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DEPARTMENT OF REVIEWS

The Journal will make an especial feature of the review of monographs and books bearing upon the field of Internal Medicine. Authors and publishers wishing to subject such material to this purpose of review should send it to the editor. While obviously impossible to make formal review of all material, an acknowledgment of all matter sent will be made in the department of reviews.

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Angina Pectoris*

A Clinical Analysis of 200 Cases

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New York City

THE following study is based upon a critical analysis of 200 cases of angina pectoris that have been carefully observed and studied over a period of a few years. We shall endeavor, therefore, to support our assertions and impressions by the clinical material at our disposal rather than by opinions or extracts from the literature.

Terminology

The term "angina pectoris" calls to mind a condition in which pain in the chest occurs in attacks, radiating frequently down the left arm and associated wtih aortic and coronary disease. The pain is substernal rather than submammary, and arrests the patient in whatever he may be doing. He becomes conscious of a sense of oppression or constriction which may reach a high grade of intensity, and even a condition of intolerable anguish. There are, in addition, characteristic associated symptoms—notably a sense of impending death, accompanied by varying vasomotor disorders such as cold sweat and deathly pallor.

It would thus seem that the clinical syndrome of angina pectoris is hardly to be mistaken. Yet the condition has a borderline of symptoms in which the picture is not so typical. These present themselves in two forms: one, in the form of what has been called "angina minor," and the other in prodromal symptoms.

Angina minor is used by us to indicate rather a transient attack of anginal pain of moderate or mitigated severity. We believe this application of the term is justifiable, although Osler applied the term to an undifferentiated group of neurotic, toxic, and vasomotor conditions in which some anterior thoracic pain was a symptom, and in which there were no signs of cardiovascular disease (1). From our present knowledge of the subject, we would dismiss the latter as a rather vague usage of the term, and employ it in the sense of mild angina pectoris.

We want to dismiss as indefensible the name "pseudo-angina pectoris" from the cardiologic nomenclature. This term particularly has no meaning. If it is applied to neurotic complaints without any organic basis, such complaints should receive their proper name. If, on the contrary, the diagnosis is not absolute, but left pec-

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toral or sternal pain is present, again the proper qualification should be made.

Prodromal Symptoms

The other group presents various prodromal symptoms which, in our observation, have eventually led up to typical attacks of angina pectoris (2). These cases are specially important and to be emphasized as they are quite common and stand the risk of being passed over as of little moment. The symptoms are often not recognized as anginal and their ominous significance is overlooked. This is particularly so because on physical examination no conspicuous cardiac signs are evident. The diagnosis in these cases must therefore be made on the subjective manifestations mainly. Altogether 83 of our 200 cases gave prodromal symptoms.

Mild prodromal attacks of angina pectoris often occur before typical attacks. The most characteristic symptom which persists often over a long period, and is as distinct evidence of the pathologic process going on behind the sternum as the anginal attack itself, is what the patients described as a "burning sensation" or a "burning pain" behind the sternum. This may be constant in the sternal region or may spread over the precordium and even to the back. Sometimes it is brought on by exertion, sometimes only by bending over, without any radiation and without any particular reference, otherwise, to the heart. A steady manubrial pain over a long period of time, or a continuous burning sensation should, therefore, be a warning signal in questionable cases. It is important to remember this symptom as part of the picture of angina pectoris. In some cases the pain is located in the epigastrium and focuses attention to the stomach. Altogether, the distress, burning, or pressing across the front of the chest, "heart-burn," or precordial pain occurred in 40 cases as a prodromal symptom of angina pectoris.

In 32 cases, for a more or less prolonged prodromal period there was noted a degree of limitation of function, usually only mild, with shortness of breath on exertion and palpitation at times. Fatigue on exertion was noted by four patients. Attacks of unconsciousness occurred in four of the 20 cases. Paroxysmal tachycardia occurred in two cases before the anginal attacks developed, and also in one case presenting signs of mitral stenosis.

These indicate that the cardiac process preceding attacks of angina pectoris is a prolonged process and that the appearance of angina pectoris is a manifestation of an already more or less developed pathology in the aorta and coronary arteries.

Tender Spots on the Chest Wall

The particular emphasis brought out by these prodromal symptoms is to indicate the nerve mechanism by which pain is produced from the aorta-coronary artery area. It is well known that impulses passing to the cord from a diseased viscus produces a disturbance in the peripheral segment to which they pass; so that any stimulus applied to the area connected by sensory nerves with the segment will give rise to exaggerated sensations. This

hyperesthesia in angina pectoris is most commonly experienced over the upper intercostal regions and the sternum, but it may be ascertained to be present over part of the neck and arm as well.

Tenderness may be discovered by the application of varying degrees of pressure with a blunt or with a sharp instrument, or by gently pinching the skin with the finger and thumb. We have endeavored to use uniform pressure by means of the thumb or the tip of the finger over the sternum and the ribs on each side, to elicit hyperesthesia or tenderness. Suddenly, the patient will assert a degree of tenderness over a certain point. This can be recorded, as we have done, by a circle painted with tincture of iodine. Several spots may thus be elicited and the chest then photographed for future reference (3).

Of the 200 cases examined, in 65 tender spots on the chest wall were unmistakably present. These often persisted continuously and increased following an attack. They were present in the right pectoral region in 33 cases, left pectoral region 24, precordial 39, sternal 7, epigastric 6, left interscapular 2, right interscapular 2.

Cause of Attack

Whether the pain has its origin in the aorta or in the heart, it is generally accepted that it is primarily determined by vascular disease—i. e., by disease affecting the base of the aorta or the coronary arteries. Although innumerable theories have been advanced to explain the occurrence of angina pectoris, the immediate cause of these attacks is still unestablished. Whether the attack follows only increased pressure in the aorta with tension exerted upon the adventitia, as Allbutt insists (4); or whether the pain results from extreme tension of the ventricular muscular walls as Mackenzie asserts (5); or whether it is due to a cramp of the heart muscle as Heberden who first described the condition believed (6); or of the coronary artery producing transient ischemia of the heart muscle (7); it is difficult in any particular case to decide.

Still another, though infrequent cause, for the onset of angina pectoris must be mentioned. We refer to the condition known as "heart strain" with symptoms of angina pectoris immediately following (8). By "heart strain" is meant an organic condition associated with the sudden development of symptoms referable to the heart and aorta which can be attributed to some unusual muscular effort or overexertion, and which result in physical disability of varying degree and duration.

With the varying pathological conditions that exist in each case, each of these may be the one explanation applicable in any particular case. In general, the causes may be classified on a theoretical basis as follows:

A. Cardiodynamic causes.
   1. Tension of the ventricular walls (Mackenzie)
   2. Cramp of the heart muscle (Heberden)

B. Vascular causes
   1. Tension of the adventitia of the aorta (Allbutt)
   2. Intra-aortic pressure changes.

3. Spasm of the coronary artery.
4. Coronary occlusion.

C. Mechanical causes
1. Interference by gastric distention and high diaphragm.
2. Reflex effects from subdiaphragmatic viscera
3. Postural and respiratory effects.

D. Toxic causes producing any of the above effects.
1. Tobacco
2. Coffee
3. Toxic pressor substances in the blood.

E. Heart strain and the effects of exertion.

Age and Sex

But there are certain etiologic factors which deserve more particular consideration. The age of onset in the group of 200 cases studied is shown in Table I. Almost 22% of the cases with angina pectoris had their first typical attack before the age of 40. It is important to recognize this fact, and not to dismiss as insignificant complaints of pain referable to the heart in young individuals. The largest number of cases began in the fifth decade in men, and in the sixth decade in women. Above the age of 60 years, the onset of angina pectoris was infrequent. The reason for this may be that a first attack occurring later in life is sooner fatal.

Table I—Age and Sex Incidence

Age	Males	Females	Total	Percent
30-40	35	8	43	21.5
41-50	62	16	78	39.0
51-60	38	17	55	27.5
61-70	16	6	22	11.0
71-80	0	2	2	1.0

There is a discrepancy in the age fractions between the grouping of cases of coronary sclerosis as found by autopsy and those of angina pectoris; indicating that in a certain number of cases the anginal picture may be due to disease of the aorta alone, and that many cases of coronary sclerosis will not have any symptoms of angina pectoris. Thus, in an analysis of 86 cases of coronary sclerosis proven by autopsy, Willius and Brown found that only 30 cases (34%) had had attacks of angina pectoris (9). In their series of coronary cases, the largest number occurred in the eighth decade.

It is well known that males are more likely to develop angina pectoris than females, and in our group the number was 151 males and 49 females. In previous reports in the literature the proportion of females is even smaller than in the series recorded here. The cause of this difference of sexual susceptibility lies mainly in the greater protection in women of the thoracic aorta from physical strain. On the other hand, all the women in our series did have severe and sudden stresses in their life as a causative factor.

Infectious and Toxic Causes

It would seem that the acute infectious poisons such as those of rheumatism and other infectious diseases deserve recognition as important causes initiating vascular changes in the aorta and coronary artery area in early middle age (10). This is

evidenced in our table in which 79 out of the total 200 cases gave a history of recurring tonsillitis; and in 11 a positive history of acute articular rheumatism with fever was obtained. Fifty-seven of the cases gave a history of rheumatic pains as a conspicuous complaint. As a direct cause of angina pectoris, therefore, we believe with Allbutt that rheumatism has not been sufficiently emphasized. Recent research has indicated that the rheumatic poison leaves its effects on the various tissues and organs and that the aorta partakes in the general reaction, with resulting rheumatic lesions (11).

The importance of syphilis as a cause seems, on the contrary, to have been overstressed. In our series, in only 8 cases was the blood Wassermann test or the history of syphilis positive. The test was negative in 44 cases and not done in 148 unquestionable cases.

Diabetes alone ranks next in frequency as an etiologic or associated factor (12). The diabetes itself may be due to arterial changes in the viscera and in that way need not bear a purely casual relationship to the cardiac lesion. It was present in 23 cases of this series.

We have been gratified in the treatment of the cases that have their etiology in syphilis and diabetes in obtaining considerable benefit from the adequate treatment of the underlying conditions. We believe with many, in continuing intensive and persevering anti-syphilitic treatment indicated in these cases (13). Concerning diabetes, we have had a number of patients whose attacks were completely abated in consequence of insulin therapy, after which the usual palliative measures, or nitroglycerine, for the attacks were entirely dispensed with.

It is doubtful whether tobacco and even alcohol are primary and very important causes, although I believe they cannot be excluded as contributory factors. The question remains unanswered whether the use of tobacco leads to arterial disease. If it does, it may of course provoke aortic lesions out of which angina pectoris may arise. The existence of a type of angina pectoris apparently following the excessive use of tobacco suggests the possibility of a direct relationship (14).

Arteriosclerosis and Blood Pressure

There is no other pain than that of angina pectoris which points with such deadly directness to arteriosclerotic disease (15). In an otherwise negative physical examination it is essential to search with untiring zeal for evidences of arterial changes elsewhere in the body. These will often indicate, in the absence of other signs, the underlying process producing the symptoms of angina pectoris.

Particular attention must be paid to the discovery of tortuous peripheral vessels. Careful inspection and palpation of the temporal and radial arteries should not be omitted in the clinical examination. Visualization of the retinal arteries is often a valuable clue. Capillary arterial changes are indicated by the presence of pericorneal arcus—the so-called "arcus senilis," and by the capillary changes

in the base of the finger nail seen under slight magnification. The effects of arterial disease manifest themselves in an equally apparent way by sclerotic changes in the kidney, producing albuminuria and casts in a urine of low specific gravity.

In our series there were noted tortuous peripheral vessels in 33 cases, and definite pericorneal arcus was present in 35 cases. Albumin or casts were present in 67 of the 200 patients studied.

frequently patients with extremely high arterial tension will remain free from chest pain or angina pectoris.

As seen from Table 2, 82 cases showed a systolic pressure below 140 mm. Hg. which must be considered entirely within the normal; 116 had a systolic pressure above 140; the majority of these, however, were below 180. The same relation seems to hold true for the diastolic pressure. In 93 cases of this series, the diastolic pressure was below 90 mm. Hg., and

TABLE II—BLOOD PRESSURE

Systolic	No. Cases	Per Cent	No. Died	Per Cent	Diastolic	No. Cases	Per Cent	No. Died	Per Cent	Pulse Pressure	No. Cases	Per Cent	No. Died	Per Cent
Below					Below					Below				
120	24	12.	3	12.5	70	9	4.5	0	0.	40	31	15.5	3	10.
121-140	58	29.	7	12.0	71-90	84	42.	13	15.	41-50	53	26.5	5	9.
141-150	37	18.5	4	10.8	91-100	64	32.	7	11.	51-60	41	20.5	9	22.
151-160	23	11.5	3	13.	101-110	23	11.5	5	22.	61-70	26	13.	3	7.
161-170	14	7.	4	57.	111-120	9	4.5	1	11.	71-80	15	7.5	3	20.
171-190	20	10.	3	30.	121-140	7	3.5	1	14.	81-90	18	9.	2	11.
191-up	22	11.	3	27.	141-up	2	1.	0	0.	91-130	14	7.	2	14.

It is already recognized that no direct etiologic relation exists between arterial pressure and the production of angina pectoris. It is, therefore, to be reasoned that a primary increase in blood pressure is not the essential etiologic factor in the production of atheroma in the aorta or the coronary arteries. We must rather assume that this vascular area at the base of the heart in certain cases undergoes morbid changes as the result of the same toxin which produces a hypertensive effect upon the rest of the vascular system. In this relation, it is interesting to note how

in 105, above 90—the majority below 110 mm. Hg. As a group, the female cases presented similar data.

Nor is there indicated from the table any particular prognostic significance of the blood pressure. The largest percentage of the cases that died had normal systolic, diastolic, and pulse pressures.

The pulse pressure as well is of little correlative importance in these cases. Of course, when seen in different phases of coronary involvement, a great variation in pressure is to be noted. The largest number of cases (94 in this series) presented

a pulse pressure between 41 and 60 mm. Hg. which may be considered entirely normal.

The group of cases with diabetes showed no special variation from the general ratios as regards the blood pressure.

Cardiac Signs

Cardiac signs are, for the experienced examiner, not difficult to recognize. But they are, in every case, a matter of interpretation. The same thrill may have several meanings, and so each of the sounds and murmurs has its own significance in any particular case. Certain signs in the physical examination of cases of angina pectoris are often dismissed, we believe, without sufficient interpretation.

First Apical Sound

To the careful examiner, the quality of the first sound has an important meaning. In 62 cases, the first sound had a poor muscular quality. This is entirely a matter of individual interpretation. The muscular quality of the heart sound is of a certain pitch and volume normally. It may, of course, be exaggerated by certain nervous influences and it may be lessened under certain conditions. In cases of myocardial disease it is often much below the normal (62 of the cases). Often, it is out of proportion to what one might expect from the visible and palpable apex beat. This deficiency of the sound, when the heart beat is very marked to palpation (2 cases) is especially significant since it occurs in cases of aneurysm of the left ventricle.

In two of the patients, we observed a peculiar hollow tone, or as we have pictured it to ourselves at times, a "relaxed drum membrane" sound. This occurred in cases of serious myocardial damage.

Rough Systolic Murmur

In our series the most commonly found physical sign was a rough systolic murmur heard usually at the base. This was present in 57 cases. This murmur over the aortic area was not marked or otherwise transmitted in 20 cases. It was heard at the apex as well in 37 cases, retaining the same rough character. It was heard only at the apex in 15 other cases. When this occurs the murmur must not be interpreted as one due to mitral regurgitation, but must be considered due to disease in the aortic valve or suprasigmoid area. We believe this is quite important inasmuch as it indicates a change in the aorta when other signs of cardiac involvement to account for angina pectoris are absent. The mechanism in the left ventricle for the production of this murmur is the same as that for mitral regurgitation, although the murmur is more likely conducted toward the base in the aortic cases.

There were also found eight cases of aortic regurgitation and three cases of aortic stenosis.

Mitral Valvular Sclerosis

Sclerotic changes in the mitral valve are quite common. In 20% of the cases of proven coronary sclerosis both the aortic and mitral valve were the seat of sclerosis or fibrosis. The

aortic valves were alone involved in another 20% of the cases, and the mitral valves alone in 7%. The appreciation of the relative frequency of sclerosis and fibrosis of the cardiac valves associated with coronary sclerosis should aid one in interpreting the auscultatory findings, especially in older individuals. Only too often the murmur noted with cardiovalvular sclerosis is wrongly interpreted as indicating chronic valvular endocarditis.

Mitral Stenosis

We have selected six cases of angina pectoris that presented the physical signs of mitral stenosis (table III). These patients all had cardiovalvular symptoms for some years prior to the onset of the angina pectoris. As indicated by the table in four of these cases, the valvular lesion followed an attack of acute articular rheumatism and is therefore to be considered of the usual rheumatic type. The diastolic blood pressure in these cases was below 100, and the systolic pressure not unusually high. In one of the patients, aortic regurgitation was associated, and the angina proved fatal within two years after the onset of the attacks.

In these cases, the electrocardiographic changes were those to be associated with mitral stenosis, and in three of these there was an inversion of the T wave in lead III. One patient had auricular fibrillation and attacks of auricular flutter, and another had paroxysmal tachycardia. Five of the cases showed characteristic tender spots on the chest wall, as in angina pectoris.

Considering the very large number of cases of mitral stenosis that we see, it is evident that only a very small proportion present the clinical syndrome of angina pectoris.

Other Significant Signs and Symptoms

Of particular significance are the associated clinical symptoms that have a definite import. These consist of paroxysmal attacks of cardiac asthma, the presence of gallop rhythm at the apex of the heart, and the occurrence of cyanosis on exertion or with the attack.

Cardiac asthma cannot be directly related to angina pectoris. It occurred only in those ten patients who already showed very extensive myocardial disease. Five of these patients died. It is therefore a phenomenon associated with the advanced changes following coronary thrombosis, rather than with angina pectoris as a clinical picture. It may be considered, like pulsus alternans, a manifestation of myocardial damage. In our series of cases, 13 cases showed marked pulsus alternans, 4 with cardiac asthma and 6 of which terminated fatally.

The occurrence of systolic gallop rhythm is a clinically ominous sign. It is an indication of myocardial deficiency and is usually associated with other evidences of beginning heart failure. It occurs more frequently in diffuse myocardial lesions and is probably parallel in its implication to the occurrence of pulsus alternans in cases of hypertension. Under adequate treatment by rest and cardiac stimulation, it may subside and re-

TABLE III—MITRAL STENOSIS GROUP

Name and Sex	Age of Onset of Angina	Tonsillitis	Rheumatism	Symptoms of heart lesion	Blood Pressure	Associated Conditions	Electrocardiogram	Tender Spots	Mortality
F.B. F.	51	+	Acute articular	30 yrs.	146 92	Tenderness over gall bladder region	T wave slightly inverted in lead III	Gall bladder tenderness	
L.C. M.	38	+	Muscular pain	5 yrs.	132 84	Paroxysmal tachycardia. Congestive nephritis	P wave notched in lead III; peaked in leads I and II	Precordium. Right pectoral region.	
J.G. M.	45	0	Acute articullar	32 yrs.	130 70	Aortic regurgitation. Tortuous vessels. Chronic nephritis.	0	0	+
B.K. F.	39	0	0	14 yrs.	104 94	Auricular fibrillation or flutter. Pulmonary asthma. Congestive nephritis.	Right ventricular preponderance. Auricular fibrillation and flutter	Sternal spots	
L.S. F.	38	+	Acute articular	3 yrs.	152 100	Pulmonary asthma. Congestive nephritis	P wave notched in lead II. T wave inverted in lead III	Precordial Epigastric	
J.W. M.	42	+	Acute articular	7 yrs.	154 96	Congestive nephritis	Left ventricular preponderance. P wave wide in lead II T wave inverted in lead III	Precordial	

appear only as evidence of increasing cardiac embarrassment.

With coronary closure, a very characteristic and most important sign is the peculiar hue of the skin that develops. It had been described by Sansum several decades ago in association with aortic valvular lesions, but no doubt was due, as we now know, to the coincidence of coronary thrombosis (16). The color consists of a sallow pallor with an ashen gray or leaden cast. It invariably signifies the closure of a branch of the coronary artery with myocardial infarction, and on that account bespeaks a grave prognosis.

Another important sign is that which we have observed at the time of the occurrence of coronary closure; i. e., the presence of definite cyanosis during an attack of angina pectoris. Ordinarily, with the attack the associated vasomotor changes produce extreme pallor with, perhaps, a cold sweat. But when cyanosis takes place, it implies a great cardiac embarrassment and is doubtless, as we have found in our cases, the result of coronary closure.

Gall Bladder Disease

The relation of angina pectoris to gall bladder disease requires careful clinical consideration. The symptom in common between the two is pain, often distressing, and localized in the epigastric region. We believe that the diagnosis may be made both of angina pectoris and gall bladder disease when symptoms pointing to both conditions are present. We are fortified in this assumption by the analysis of Willius in which he found chronic cholecystitis, with or without stones, in 26% of proven coronary cases. This high incidence is due to the fact that gall bladder affection manifests itself in middle or later life when arterial degenerative changes become evident. The error most often committed is one of omission; where the gall bladder disease is neglected and the diagnosis is made of angina pectoris alone.

In our series, gall bladder disease was associated with angina pectoris in ten of the 200 cases.

Electrocardiographic Studies

The constant presence of myocardial changes in cases of coronary involvement would lead one to suppose that the electrocardiogram would be of great assistance in diagnosis. Of course, if we were to expect spectacular changes in the electrocardiogram in every case we would find ourselves not fully satisfied. Looking at it critically, however, one is not disappointed. It is true that occasionally, where the clinical symptoms are prominent, the electrocardiogram will appear normal; or again, when the patient is in apparent good health, the electrocardiogram will be gravely informative.

The changes that take place in the electrocardiographic picture immediately after coronary thrombosis will naturally vary with the location of the involved coronary vessel and the size of the branch. (Compare figs. 1 and 2.) Certain characteristic alterations develop in different cases because of the greater frequency of clos-

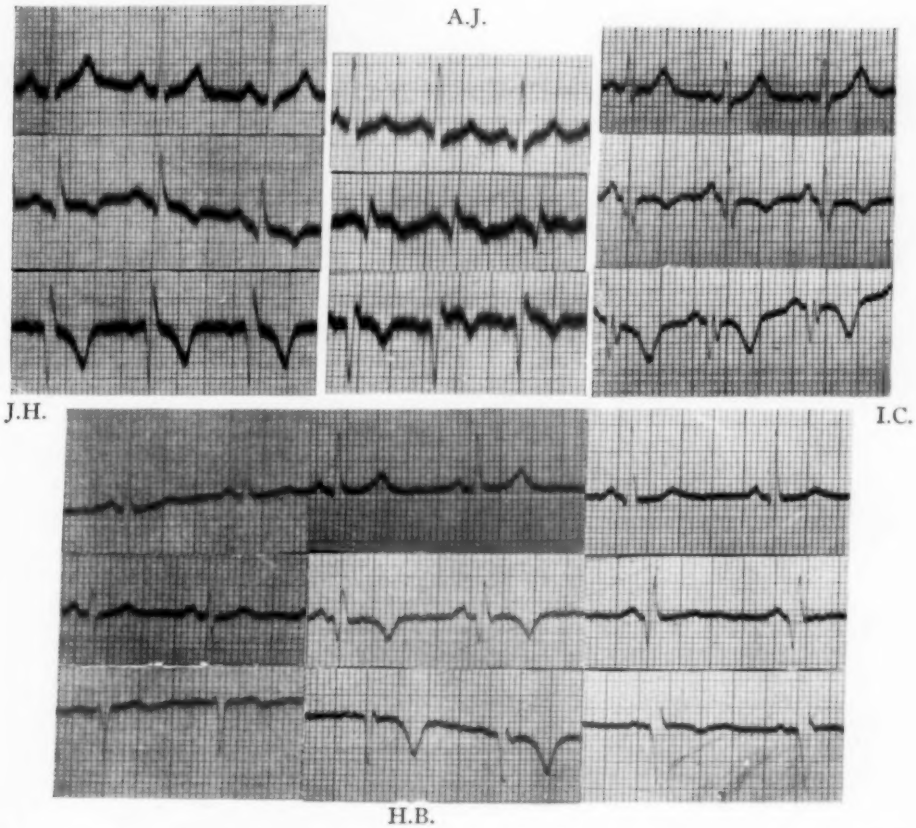

FIGURE 1.—Four cases showing characteristic inversion of the T wave in leads II and III after a severe attack of angina pectoris.
Case J.H.—Four days after severe attack, 18 months after onset.
Case A.J.—Three weeks after first attack. Sudden cardiac death two months later.
Case I.C.—One week after first attack.
Case H.B.—Six months after onset of pain.
Eight months later—one week after first attack.
Eighteen months later—cardiac death six months later.

ure of the anterior descending branch of the left coronary (17). It is probable that a comparable series of pathologic changes takes place within a variable period of time. With extensive infarction of areas in the heart and especially of the endocardial regions, more marked electrocardiographic evidence is produced, such as bundle branch block, QRS widening and notching, etc.

Transitory electrocardiographic effects may be produced in organic coronary lesions where the coronary closure was not complete. (Fig. 3.) They may also occur synchronously with functional changes in the coronary circulation (18).

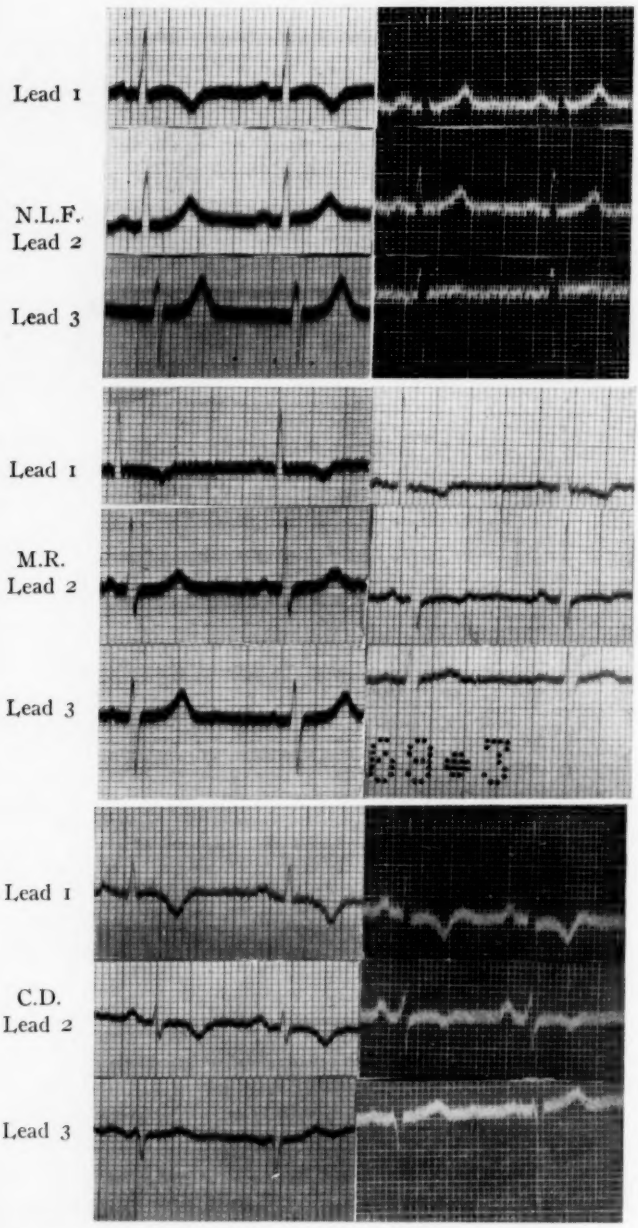

FIGURE 2.—Three cases showing characteristic inversion of the T wave in lead I after severe attack of angina pectoris.
Case N.L.F.—Two weeks after his first severe attack.
Four years later.
Case M.R.—One month after his first attack.
Three years later.
Case D.D.—Three weeks after first severe attack.
Two and a half years later—no intervening severe attacks.

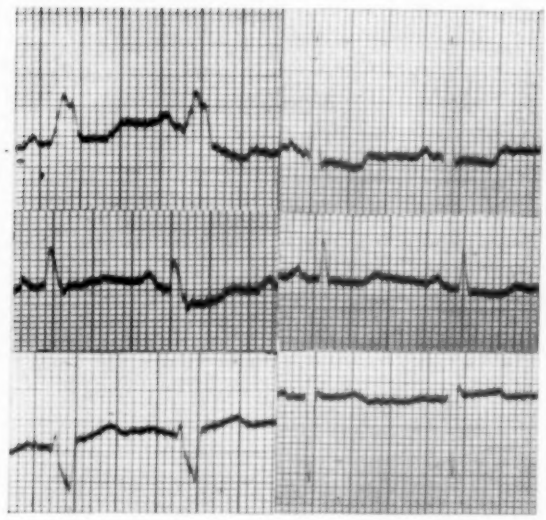

FIGURE 3.—Case R.H., five weeks after her first severe attack. One year later—no intervening attacks.

Of the 200 patients examined, a rather broad analysis was made of the electrocardiographic films. An exact tabulation could not be made for the reason that in many cases repeated films were recorded at intervals of months and years; and these often showed remarkable differences one from the other. However, certain general results can be analyzed from the table (table IV).

There were 110 cases with left ventricular preponderance and only six cases of right ventricular preponderance, while 58 had no ventricular preponderance. The mortality was not appreciably greater in any one of these groups.

It would seem that the importance of widening of the QRS wave, which indicates a time obstacle in the conduction of the stimulus, is equal in its significance to the notching and thickening of the QRS wave, even when it is present in lead III. As is to be seen, of each of the groups showing either of these changes, six or 25% died.

Judging from the table, the prognostic significance of low voltage is not as great as of high voltage in the cases of angina pectoris. Of the seven cases with high voltage, 42% died; of the eight cases with low voltage, 25% died (19).

Inversion of the T wave in leads I and II, and in leads II and III are of equal significance, although a smaller number of the cases showed these combined changes. The T wave was inverted in lead I alone in 22 cases, and in lead III alone in 53 cases. But the fatalities that occurred were greater in percentage when the T wave was inverted in two leads simultaneously.

Of course, with bundle branch block and heart block, which indicate extensive myocardial changes involv-

TABLE IV—ANALYSIS OF ELECTROCARDIOGRAMS

	Number	Number Died	Percent Died
Left ventricular preponderance	110	12	11%
Right ventricular preponderance	6	1	16%
No ventricular preponderance	58	10	17%
Sinus bradycardia	2	1	50%
Sinus tachycardia	3	1	33%
P wave inverted, notched, or widened	22	2	9%
QRS wave notched and thickened	22	6	27%
QRS wave widened	24	6	25%
Extrasystoles—Auricular, ventricular, nodal	15		
Bundle branch block	3	2	66%
Complete heart block	1	1	100%
T wave inverted in lead I only	22	1	4%
T wave inverted in leads I and II	7	2	28%
T wave inverted in lead III only	53	5	9%
T wave inverted in leads II and III	10	2	20%
Low voltage of QRS complex	8	2	25%
High voltage of QRS complex	7	3	42%
Electrocardiogram negative	12	2	16%

ing the subendocardial tissues, the mortality was very high.

It is well known that electrocardiographic changes follow promptly upon an attack of angina pectoris associated with coronary closure (20). In the series of prints shown in Fig. 1 and 2, the time relation is indicated between the attack of angina pectoris, implying coronary closure, and the electrocardiograms taken. The electrocardiograms, arranged in a series, show the changes that take place with infarction and with reparation. Sharp inversion of the T wave may take place either in lead I or in lead III, following a severe attack of coronary closure. The lead involved may possibly have a relation to the vessel affected. This, however, cannot be asserted with any certainty at the present time, as further study of these cases is necessary. However, the prints and legends are presented here for the great interest that they excite, and the conspicuous changes that are so apparent (fig. 4).

MORTALITY

One group of our series that offers considerable interest in its analysis is that of 30 patients with angina pectoris who have died during the period of our observation. These patients had been seen a varying length of time and were carefully studied. The age of onset had apparently a good deal to do with the duration of life while suffering angina pectoris. Patients whose first anginal attack occurred before the age of 40 showed a life expectancy of between 6 and 9 years before death occurred. Above 40, the duration was from one to three years. Above 50, the average duration was considerably lower; and above 60 it was less than six months. This is very significant, and suggests that the arteriosclerotic process can go

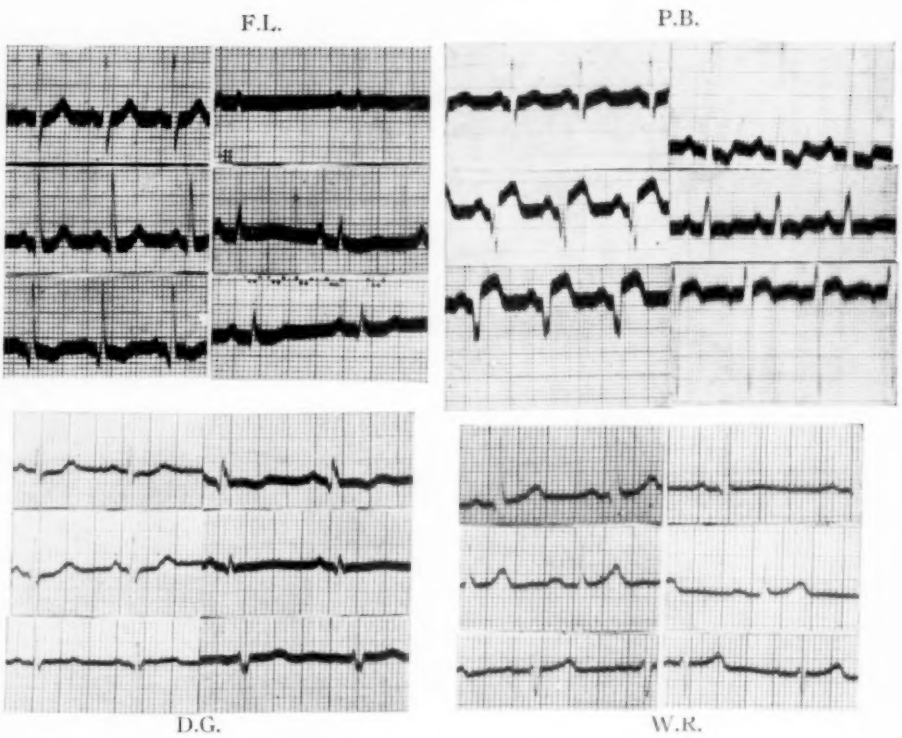

FIGURE 4.—Case F.L., four months after first attack—two days after severe attack.
Three months later—five days after severe attack.
Case P.B.—Four weeks after onset.
Ten days later.
Case D.G.—Five years after first attack; one week after third severe attack.
One year later, six months after last severe attack.
Case W.R.—One week after first attack.
Three months later.

on for a long time unobstrusively and death result only when the lesion is well advanced at a later age. However, in 13 of the patients who died after a relatively short time of clinical angina pectoris, there were present prodromal symptoms that had lasted from one to ten years. This emphasizes the importance of giving attention to the prodromal symptoms of cardiac arteriosclerosis.

The electrocardiograms in the cases that died were also very instructive. In a few of these no other evidence of myocardial damage was present except left ventricular preponderance. However, in a large number, there was notching of the QRS wave, inversion of the T wave in leads I and II; or II and III, or in either I or III. QRS notching and widening was quite common. Two cases showed bundle branch block, and one case presented heart block.

SPECIAL METHODS OF TREATMENT

Of recent years, palliative measures have been used in some cases with

considerable benefit for angina pectoris. These consist of methods which endeavor to reduce the amount of pain felt, either by actually altering the pathologic process in the aorta and coronaries, or by blocking the pain stimuli from the diseased area. In the first instance, I refer to the use of diathermy.

Diathermy

Diathermy is a form of treatment in which heat is generated in the tissues by the passage through them of high-frequency currents. It is essentially different from the warming of a part or the application of heat to the skin. Human tissues are conductors of an electric current, but they are conductors with a high resistance, and consequently the passage of an electric current through them generates heat. In February, 1912, Nagelschmidt published his classical paper in the Roentgen Ray Archives on the diathermic treatment of circulatory disorders, re-

Table V—Deceased Group

Name and Sex	Age at Onset	Age at Death	Duration	Time of Prodromal Symptoms	Electrocardiogram	Significant Signs and Symptoms
I.B. F.	48	54	6 yr.	0	Extrasystoles	Aneurysm heart?
P.B. M.	54	54	1 mo.	0	Left ventricular preponderance. QRS wave notched. T wave inverted in leads I and II	
M.B. M.	50	52	2 yr.	9 yr.	T wave inverted in Lead I. QRS wave notched and widened.	
H.B. M.	46	49	3 yr.	0	Three successive electrocardiograms showing coronary closure	Cyanosis at times
P.C. M.	54	57	3 yr.	0	QRS wave notched and widened. T wave shows low voltage.	Pulsus alternans. Cardiac asthma
L.F. F.	58	59	1 yr.	3 yr.	Right bundle branch block. Arborization block.	Pulsus alternans. Cardiac asthma
A.G. M.	36	43	9 yr.	0	Left ventricular preponderance.	Cyanosis at times
J.G. M.	45	47	2 yr.	0	0	Mitral stenosis. Aortic regurgitation
A.H. M.	45	47	2 yr.	0	Negative.	Wassermann ++++

TABLE V—CONTINUED

Name and Sex	Age at Onset	Age at Death	Duration	Time of Prodromal Symptoms	Electrocardiogram	Significant Signs and Symptoms
G.H. M.	57	61	4 yr.	11 yr.	0	Cardiac asthma
A.J. M.	65	65	3 mo.	0	Left ventricular preponderance. T wave inverted in Leads II and III	Auricular fibrillation. Aortic stenosis
I.L. M.	52	54	2 yr.	2 yr.	Left ventricular preponderance.	Gallop rhythm
S.L. M.	39	41	2 yr.	0	Left ventricular preponderance. T wave inverted in lead III. QRS wave notched and widened.	First sound much weaker than diffuse impulse
A.L. M.	61	61	6 mo.	15 yr.	Left ventricular preponderance. T wave inverted in leads II and III	
J.M. M.	33	39	6 yr.	0	0	Pulsus alternans. Cardiac asthma
R.M. F.	75	76	1 yr.	0	0	Auricular fibrillation. Sudden death
G.M. M.	56	64	8 yr.	2 yr.	P wave wide and diphasic in lead III. QRS wave diphasic in leads II and III. T wave inverted in leads II and III.	Sudden death
S.M. M.	46	47	1 yr.	8 yr.	Left ventricular preponderance.	Aneurysm of left ventricle.
J.P. M.	65	65	3 mo.	1 yr.	Left ventricular preponderance. T wave inverted in lead III	
I.P. M.	56	59	3 yr.	0	Right bundle branch block.	Pulsus alternans
I.P. M.	50	52	2 yr.	0	T wave inverted in Lead I.	Hypertension. Cerebral arteriosclerosis.
M.R. M.	40	49	9 yr.	0	Right ventricular preponderance. Low voltage. P wave notched in lead I and high and wide in lead II.	Frequent cyanosis Cardiac asthma. Cheyne-Stokes respiration.

TABLE V—CONTINUED

Name and Sex	Age at Onset	Age at Death	Duration	Time of Prodromal Symptoms	Electrocardiogram	Significant Signs and Symptoms
L.R. M.	60	60	6 mo.	2 yr.	0	
T.R. M.	54	56	2 yr.	2 yr.	Left ventricular preponderance. QRS wave notched and widened.	Pulsus alternans. Generalized atherosclerosis
R.S. M.	63	63	3 mo.	2 yr.	0	
A.S. M.	49	54	5 yr.	0	Left ventricular preponderance. Bradycardia QRS wave widened. T wave inverted in lead III.	Pulsus alternans. Cerebral sclerosis
M.S. M.	43	44	1 yr.	10 yr.	QRS wave notched. T wave inverted in lead III.	
M.S. M.	57	65	8 yr.	2½ yr.	Left ventricular preponderance. P wave inverted in lead III.	
W.S. M.	51	53	2 yr.	0	Left ventricular preponderance. Heart block. QRS wave wide. T wave inverted in leads I and II.	Syphilitic heart block
O.S. M.	47	48	1 yr.	0	Left ventricular preponderance. P wave inverted in leads II and III.	Aortic stenosis and regurgitation.

lating numerous cases treated by diathermy. Among these were cases of intermittent claudication where the effect of suggestion could be fairly eliminated; and the result of the diathermy was effective.

In cases of angina pectoris, the current has been applied to the chest, "through and through," in the hope that the coronary circulation might be improved. It is probably successful only to a varying degree where vascular spasm is a factor in the raised pressure (*22*). Diathermy may produce temporary dizziness and faintness or cause excessive sweating, and must therefore be used with a degree of caution.

SYMPATHECTOMY

A number of surgical measures have been resorted to to relieve the patient of the pain inherent in the anginal attack. These procedures endeavor, in principle, to circumvent or

interrupt the course of the afferent fibres from the heart.

The great importance of the relief of pain arises not alone in the fact that the patient's suffering is reduced, but more especially in the fact that the patients with angina pectoris may die as a result of the pain by cardiac inhibition through the vagus. It must be remembered that a diseased heart is more responsive to vagus influence than a normal one (23).

In one method, alcohol injection is made into the posterior ganglion of the lower cervical and upper dorsal spinal roots (24). Section of these roots has not been attempted, but extirpation of the sympathetic cervical chain has been done in a large number of cases. In these, various parts of the sympathetic ganglion were removed, the stellate ganglion being removed in some cases on one or both sides, and the upper or middle sympathetic ganglion in other cases. Jonnesco extirpated the entire cervical chain (25). Danielopolu sectioned the cervical sympathetic chain above the stellate ganglion and injected with alcohol the ganglia of the spinal nerves (26).

No uniform result has been obtained and more complete relief reported in those cases in which most of the sympathetic cervical chain has been removed on both sides. The reports in general from each of these methods are quite favorable inasmuch as the attacks of severe precordial pain are considerably relieved and often the freedom from pain is present for months (27). Most patients of our series of cases have, however, been able to keep more or less comfortable under our observation, employing nitrites, avoiding strain, taking a light diet, and requiring occasional sedatives for the discomfort.

We feel justified in classifying our series of cases into the following groups:

1. Angina pectoris due to aortic disease.
   a. Prodromal cases.
   b. With hypertension
   c. With aortic atheroma
   d. With aortic regurgitation
   e. With aneurysm of the aorta
   f. With aortic stenosis
   g. Other pathological lesions that may exist
2. Angina pectoris with coronary disease
   a. With coronary arterial spasm
   b. Left coronary involvement
   c. Right coronary involvement
   d. Coronary capillary involvement
3. Angina pectoris with rheumatic disease
   a. Rheumatic myocarditis
   b. Mitral stenosis

Though we recognize the incompleteness and inadequacy of such a classification, we believe that it is only with a classification conceived on some organic basis that the newer problems in the study of angina pectoris can be undertaken with more discerning scrutiny.

Summary

1. Two hundred cases of angina pectoris are critically discussed.

2. The name "pseudo angina pectoris" is indefensible and should be dismissed from the cardiologic nomenclature.

3. Angina pectoris often presents various prodromal symptoms which indicate that the cardiac process preceding the attacks of angina pectoris is a prolonged one, and that the appearance of angina pectoris suggests a more or less developed pathology in the aorta and coronary artery.

4. Hyperesthesia, or tender spots on the chest wall, may serve as a differential diagnostic point from intra-abdominal disease.

5. The immediate cause for the attacks of angina pectoris is classified according to the possible pathological conditions that may exist.

6. Almost 22% of the cases had their first typical attacks before the age of 40.

7. Rheumatism and diabetes appear to factor importantly in the etiology.

8. Arteriosclerotic disease is the outstanding condition in angina pectoris as indicated by the tortuous peripheral and retinal vessels, the presence of pericorneal arcus, and arteriosclerotic renal changes.

9. There seems to be no direct etiologic relation between arterial blood pressure and the production of angina pectoris.

10. The most commonly found physical sign in angina pectoris was a rough systolic murmur due to aortic change.

11. Angina pectoris was associated with rheumatic mitral stenosis in six cases.

12. Of particular prognostic significance are the associated clinical symptoms of cardiac asthma, pulsus alternans, systolic gallop rhythm, and the occurrence of cyanosis on exertion or with an attack.

13. The differential diagnosis of angina pectoris from gall bladder disease is discussed.

14. The electrocardiographic picture in angina pectoris is analyzed in detail.

15. Thirty patients of our series died from angina pectoris. In these the age of onset bore a distinct relationship to the duration of life—the later the onset, the worse the prognosis.

16. Palliative and surgical measures in the treatment have proven of considerable value in selected cases.

17. A classification of angina pectoris is presented conceived on an organic basis which may serve for further study.

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Congenital Atresia of Aortic Ring*

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ALL congenital cardiac defects belonging to the cyanotic group, true morbus cæruleus, must be considered as very grave conditions. Perhaps the most serious of this group are those cases showing atresia or aplasia of the valvular orifices on the left side. These individuals usually die during the first few days of life and it is necessary for a compensatory anatomical adaptation to be present in order to maintain life even for a short time.

Atresias on the left side have, associated with the anomaly, defects in the ventricular auricular septum, as well as a widely patent ductus Botalli. The left ventricular cavity is very small and the wall shows an eccentric hypertrophy. There is an accompanying small left auricle. The right ventricle and auricle are enormously dilated and hypertrophied. Usually the right ventricle is crescent shaped and surrounds the whole lower portion of the left ventricle, thus causing the apex to be entirely formed by the right heart. Invariably the pulmonary artery is greatly enlarged in direct contrast to the ascending portion of the aorta which is markedly hypoplastic. Often we have accompanying anomalies in other parts of the body such as transposition of the viscera, an absent spleen or kidney.

Many varied theories have been advanced in regard to the etiology of cardiac defects. However, we can be safe in dividing these anomalies into two definite groups with reference to their cause—I, arrest of growth, II, fetal disease. Undoubtedly a large percentage is caused by some disturbance in development at different stages of fetal life. On the other hand, we can prove conclusively that cardiac anomalies are frequently caused by some inflammatory or degenerative process being present during fetal life. It has been shown that syphilis plays a very active part in the causation of many cardiac defects.

Previously it was thought that fetal endocarditis played the most active part in fetal disease and that myocardial changes were of little significance. In recent years microscopic pathology has proven that myocardial disease is by far the most common cause of cardiac anomalies excluding those due to primary arrest in development. Abbott states, in a very masterful discussion regarding the etiologic factors of cardiac defects,—"Fetal endocarditis probably occupies a very minor rôle, being limited to those relatively few cases in which a rheumatic

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endocarditis is directly transmitted from the mother to her offspring. Of far greater importance are undoubtedly the myocardial changes which occur as a result of congenital syphilis or other infection carried in the coronary stream." Most cases of atresia of the orifices reveal in the myocardium different degrees of degeneration, vacuolation, fatty change, and diffuse fibrosis often myxomatous in character, very similar to that described by Warthin as "focal fatty degeneration associated with localized colonies of spirochaeta pallida." Observations by von Zalka in six cases of atresias or stenosis of the aortic and pulmonic orifices agree with the above findings. In every case of this group definite myocardial changes are found.

Aortic atresia is not common. Those forms due to lack of development are distinguished from those caused by inflammatory processes. The inflammatory forms are the more frequent, occasionally due to fetal endocarditis with fusion of the cusps but more often due to a diseased myocardium with a narrowing of the conus and obliteration directly below the orifice. Simmon's report states that the infant attained an age of sixteen weeks but this subject is the oldest on record, the average age being approximately three weeks. Undoubtedly there have been many similar cases which perished during fetal life or shortly after birth and were never recognized.

The literature contains six cases of aortic atresia. To this we add the present communication — a case of aortic and mitral atresia associated with a widely patent foramen ovale and a dilated ductus arteriosus.

History of Case: The mother came to hospital 5-20-28 stating that she was pregnant and that her last menstrual flow was in August 1927. Physical examination showed her to be very near term. She was a well nourished individual, seventeen years of age and married. No previous pregnancies or miscarriages had occurred. There was no clinical evidence of syphilis and her blood Wassermann was negative. She had always been in excellent health.

Labor began at 10 P. M., 5-21-28, and lasted seventeen hours. Presentation was a complete breech. The feet were delivered by the Pinard manuever and the body was delivered spontaneously. Weight at birth was 2820 gms.

Immediately after delivery the child breathed and cried naturally. There was a slight cyanosis of the nails and mucous membranes but the skin of the body was a natural pink. Externally there were no deformities or abnormalities with the exception of the scrotum which was red and swollen. The following day the infant was apparently progressing favorably and no cyanosis was noted. From the start it took to the breast poorly but otherwise gave no cause for alarm until the second morning when cyanosis was first noted. This symptom appeared gradually and steadily increased in intensity. At first, only the extremities and mucous membranes were affected but soon there was a generalized bluish discoloration of the whole body surface. Oxygen was administered every alternate ten minutes but with no good result. The infant was carefully examined at this time. Very rapid and slightly irregular heart sounds were heard but there was no suspicion of a congenital heart lesion being present. Intermittent dyspnoeic attacks began to occur late in the second day and recurred at intervals until death one day later. During these attacks of respiratory embarrassment the cyanosis became much more marked. Death took place 5-25-28, sixty-two hours after birth.

Wassermann reaction on the cord blood was negative.

Autopsy performed 20 hours after death. Protocol (abbreviated). Baby M. Sex—Male. Age 62 hours.

External Examination: Body is that of a well developed male infant 47 cms. in length and weighing 2670 gms. Nutrition appears good. The head is symmetrical and measures bi-parietal diameter 9½ cm. Occipito-frontal 10½ cms. The thorax and abdomen appear normal. No anomalies or deformities are present and careful examination reveals no evidence of birth trauma. The skin shows a generalized purplish discoloration due to marked cyanosis; this is more intense over the dependent portions. Mucous membranes also are markedly cyanotic.

Head: The brain shows a very marked congestion but there is no evidence of birth trauma.

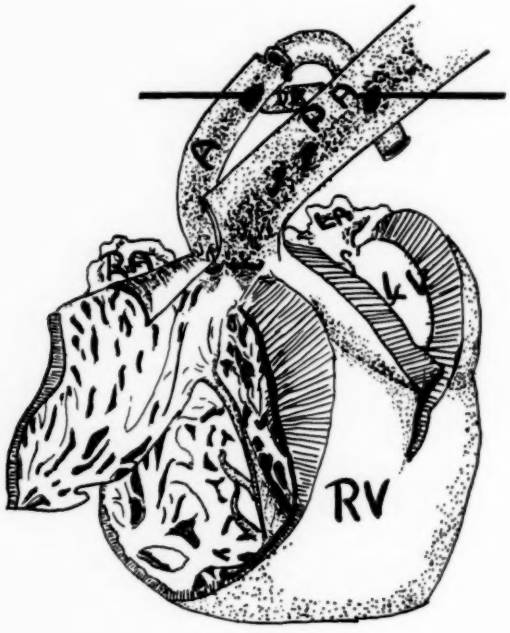
Abdominal Cavity: Contains no free fluid. All the viscera are in normal positions and no abnormalities are noted.

Thoracic Cavity: The lung borders are 2 cm. apart in the anterior mediastinum. Heart lies transversely to the left of the mid-sternal line with the apex in the 4th intercostal space well outside the mid-clavicular line and pointing toward the left axilla. Anterior mediastinum contains a globular thymus which weighs 7 gms.

Pericardium: Is normal in tension and thickness. Sac contains 3 cc. of a clear fluid.

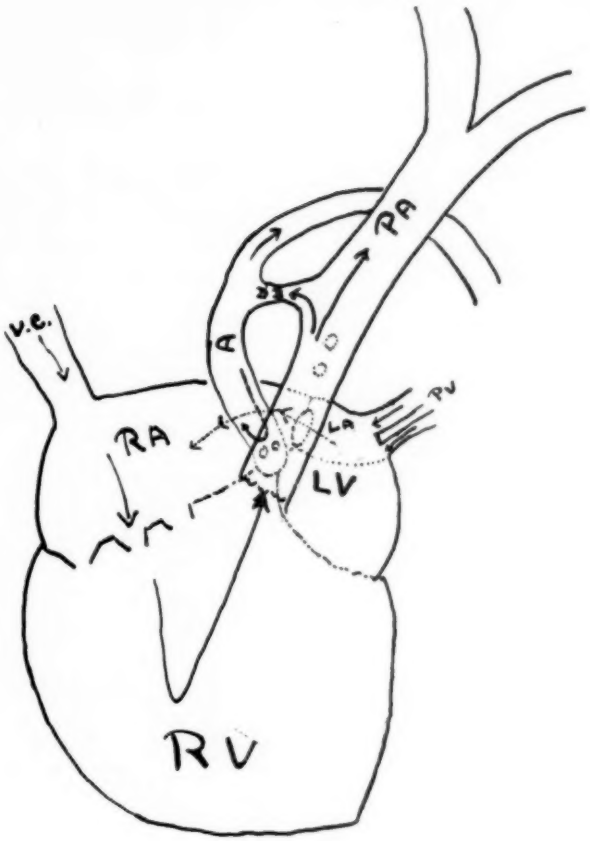
Heart: Measures 7x5x2 cm. and weighs 28 gms. Appears markedly enlarged especially on the right side. The apex is made up entirely by the right ventricle.

Left Heart: Musculature is a dull red. The left auricle is very small and contains 2 cc. of agonal clot. There is no open-



No. I.

Aortic and mitral atresia. Patent ductus arteriosus and widely patent foramen ovale. Obliteration of the aortic orifice below the cusps. Hypoplasia of aorta with marked dilatation of pulmonary artery. Hypertrophy of right ventricle and auricle. Aplasia of left ventricle and auricle. (Drawing by Miss Dorothy Wheeler.)



No. II.

Diagram to illustrate the flow of blood. Direct communication between the left and right auricles through foramen ovale. Also a widely patent ductus arteriosus joins the pulmonary artery to the aorta. Note the coronary openings above the fusion in the aortic ring. (Diagram by Miss Dorothy Wheeler.)

ing in the mitral region with the endocardium smooth and shining. A direct communication between the left and right auricles is established by means of a widely patent foramen ovale. The diameter of the opening measures 9 mm. On opening the heart the left ventricular cavity is found to be greatly diminished in size with no natural opening present; the mitral orifice is completely sealed and there is a complete atresia of the aortic ring. The muscle wall appears somewhat hypertrophied.

Right Heart: Right ventricular wall appears hypertrophied. Both cavities are enormously distended. It is noted that the right ventricle practically encircles the left ventricle and the right cavity is crescent shaped. No opening can be found in the interventricular septum. The endocardium is smooth and shining. Tricuspid valve is well formed with no thickening of the cusps. There is a marked increase in calibre of the pulmonary orifice but the cusps are three in number and appear normal. On tracing the vessel upward a widely patent ductus ateriosus is found with the opening 4 cm. from the pulmonary valve. The ductus opening measures 6 mm. and the total length is 8 mm. The pulmonary artery is enormously dilated but appears

normal otherwise. There is a branch to each lung and no anomalous vessels are noted.

Coronary Vessels: Two small openings about 1 mm. in diameter are found near the blind end of the aorta. A small probe can be passed into the lumen of either coronary vessel.

Aorta: Is hypoplastic throughout its whole course but markedly so in the ascending portion and in the arch. The opening of the ductus is in the arch near the descending portion. Diameter of the opening is 5 mm.

Lungs: Are air containing. There is a marked congestion throughout with a partial atelectasis in the lower lobes.

Microscopic Findings

Spinal Cord: There is no evidence of syphilis.

Cerebrum: Congestion and edema is marked. No localized lesions are present.

Heart: No evidence of syphilis is found. Muscle is well developed. Endocardium shows a marked thickening apparently as it approaches the aorta with complete obliteration of one vessel and nearly complete obliteration of another.

Lungs: Contain very little air. The majority of the alveolar spaces are not dilated. There is extreme congestion and edema with multiple petechial hemorrhages. (Death by asphyxia.) There is no evidence of pneumonia. The fat stains show numerous fat droplets, finely divided in the alveolar spaces.

Thyroid: A small amount of colloid is present with exception of scattered areas where it is unusually abundant for a child three days old.

Thymus: There is hyperplasia of the medullary portion with numerous corpuscles of Hassall. The lymphoid portion is not hyperplastic.

Spleen: Shows marked congestion. Some of the follicles have central lymphoid exhaustion.

Liver: Is an extreme nutmeg liver with marked central necrosis and fatty degenerative infiltration. Fat stains show marked fatty degenerative infiltration.

Adrenals: The medulla is hypoplastic. There is a slight lipoidosis of the cortex.

Kidneys: Show congestion and slight cloudy swelling (probably post mortem). Fat stains show marked lipoidosis of the loops of Henle.

Pathological Diagnosis: Congenital atresia of aortic ring with absence of aortic valve. Atresia of mitral valve. Patent foramen ovale. Dilated pulmonary artery with patent ductus arteriosus. Hypoplasia of left auricle and ventricle. Hypoplasia of aorta. Extreme congestion, oedema and hemorrhage by diapedesis in lungs. Pronounced nutmeg liver. Hyperplasia of thymus. Hypoplasia of adrenals. Generalized passive congestion. Asphyxia.

Discussion

From the clinical aspect a few features should be emphasized. Diagnosis of congenital heart disease in the early stages of life is at all times very difficult and often impossible. Though the clinical findings in this case are very definite there are two conspicuous features, cyanosis and dyspnoea, which are present at some stage of life in most cases of a similar nature.

Cyanosis in the majority of aortic atresias is very marked but one should never be misled by the absence of this sign. Peacock cites different examples of congenital defects where venous and arterial blood are freely mixed and there is no cyanosis evident. The causative factors of cyanosis are fully discussed and very adequately summarized by Abbott under the two headings of modifying and determining factors. The determining factors produce cyanosis by directly raising the concentration of reduced hemoglobin in the capillary stream above its "threshold—value," while the modifying factors may alter the degree of cyanosis but cannot by

themselves produce an increase in oxygen unsaturation. In the present case cyanosis was not marked during the first two days but it became very pronounced in the last 20 hours of life.

Dyspnoea is also a very frequent symptom in this group, especially when cyanosis is marked. It does occur, however, when no trace of cyanosis is seen and apparently there is no definite relationship between these conditions. In the terminal stages many individuals have marked dyspnoeic attacks which are accompanied by marked increase in the cyanosis. This feature is well demonstrated by the present history.

Often a harsh, systolic, machine-like murmur, accompanied by a thrill, is localized to the upper precordium in cases of patent ductus. On careful examination the clinicians were not able to elicit any such findings in the above case.

The pathologic picture gives no evidence of myocardial involvement. The endocardium is definitely thickened in the left ventricular cavity but there is no other proof of an inflammatory process. Syphilis cannot be suspected after careful microscopic examination of the different organs and of the cord and placenta. No other infective process is present in any of the viscera. We may conclude that this case appears to belong to that group of cardiac defects caused by arrest of development.

To summarize we have:

1. A case of aortic and mitral atresia which survives for 62 hours.
2. Cyanosis and dyspnoea are the prominent clinical features.
3. There is no definite evidence of an inflammatory process and the defect is probably due to arrest of development in fetal life.

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Krysolgan in the Treatment of Lupus Erythematosus: Report on Twenty-eight Cases*

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In the treatment of lupus erythematosus it is probably too much to expect that any one method will act as a specific in all form of the disease, although it can be said without hesitation that since the disease is the result of an internal toxic process, its attack by the internal and systemic route is more logical than by any local application. Many drugs have been used in the former manner, but only a few, and these probably not very effective, have attained reasonable popularity. Since the gold preparations were first used about fifteen years ago, they have gained in popularity, and for the last three or four years in this country they have been widely discussed, but use of the preparations has been delayed by the European reports on their toxic and even lethal effects. Krysolgan is seemingly the preparation most popular in Europe, and since Schamberg and Wright (1) published their report on the use of gold and sodium thiosulphate, this preparation has apparently become the choice in America. I have employed both, but since my experience with krysolgan has been greater I shall confine my discussion here to this drug.

Although I have used krysolgan in the treatment of twenty-eight cases, I shall only abstract a certain number of cases in which the results can be objectively demonstrated. In a critical estimate of the value of the drug the entire series will be considered.

Abstract of Cases

Case 1.—A man, aged forty-three, first noticed chronic discoid lupus erythematosus in October, 1925. There were no demonstrable septic or tuberculous foci. The patient was treated by the injection of foreign protein, by the application of roentgen ray to the gland-bearing areas, by the administration of quinine and iodoform for the constitutional effect; carbon-dioxide snow, lotio alba, and 3 per cent ichthyol ointment were applied locally. None of these measures produced a satisfactory response. Krysolgan was then given, this being the first time the drug was used in The Mayo Clinic. The results are shown in figure 1.

Case 2.—A woman, aged thirty-two, first noticed the lesion in February, 1926. On examination at the clinic infected tonsils were noted but no evidence of tuberculosis. Krysolgan was given with healing of the

*Submitted for publication April 26, 1928.

[1]Schamberg, J. F. and Wright, C. S.: The use of gold and sodium thiosulphate in the treatment of lupus erythematosus. Arch. Dermat. and Syph., 1927, xv, 119-137.

lesion. The tonsils were removed before her dismissal. Local treatment by ultraviolet light and roentgen ray had been given elsewhere (fig. 2).

Case 3.—A woman, aged twenty-five, first noticed the lesion on the bridge of the nose in June, 1926. Later two small patches appeared on the left cheek. There were no demonstrable pyogenic or tuberculous foci. Mild local applications were applied before krysolgan was given. It developed subsequently that the patient was in the first month of pregnancy when krysolgan was begun, but no untoward symptoms resulted (fig. 3).

Case 4.—A woman, aged sixty-one, first noticed the lesions in 1914. On examination at the clinic dental sepsis and old tuberculous lesions of both upper lobes were found. Various methods of treatment were ineffective but krysolgan was given with improvement ((fig. 4).

Case 5.—A woman, aged forty-eight, first noticed the lesions in 1921. Examination did not reveal demonstrable septic foci, but an old tuberculous lesion of the upper lobe of the lungs was noted. She had been treated by radium, Kromayer light, carbon-dioxide snow, and various medicinal applications locally, quinine internally, and roentgen rays for their systemic effect, before krysolgan was given. There was satisfactory response from krysolgan only (fig. 5).

Case 6.—A man, aged thirty-four, first noticed the lesion in 1920. His tonsils were infected but there was no evidence of tuberculosis. Treatment had consisted in large doses of quinine before the krysolgan was given. The response in this case was rather slow but finally very satisfactory (fig. 6).

Case 7.—A man, aged thirty-three, first noticed the lesion in 1921. There were no demonstrable septic or tuberculous foci. Treatment had consisted of the injudicious use of radium and roentgen rays to the point of marked atrophy and telangiectasia without materially affecting the lesion. Treatment by the administration of krysolgan produced satisfactory response (fig. 7).

Case 8.—A woman, aged twenty-three, first noticed the lesion in 1917. There were no demonstrable septic or tuberculous foci. Various methods of treatments had been instituted both for local and for systemic effect; all were unsatisfactory. Krysolgan was begun in October, 1927; the results were satisfactory (fig. 8).

Method of Treatment in the Cases Abstracted

Cases 1 to 5 show complete involution of the eruption in the sense that not a vestige possibly denoting inflammatory reaction remained. All the erythema, scaling, crusting, and epithelial plugging disappeared and only a smooth white scar, with possibly faint telangiectasia in an occasional case, remained. In Cases 6 to 8 the objective result was not quite so satisfactory. Radium had been applied to the point of permanent injury to the skin. While all active inflammatory reaction had subsided it was especially difficult to determine how much of the final condition of the lesion was due to the radium treatment and how much was due to the lupus erythematosus.

In Case 1 twelve injections were given of approximately 0.5 gm., a minimal dose of 0.0001 gm. and a maximal of 0.05 gm. The intervals between injections varied from nine to fourteen days. Considerable caution was exercised since this was the first case treated. In later cases the dosage was materially increased and the time interval decreased. It was particularly noticeable, after more experience, that the small dosage had given excellent results. In Case 2 eighteen injections, a total of 0.6 gm., were given at weekly intervals. This was

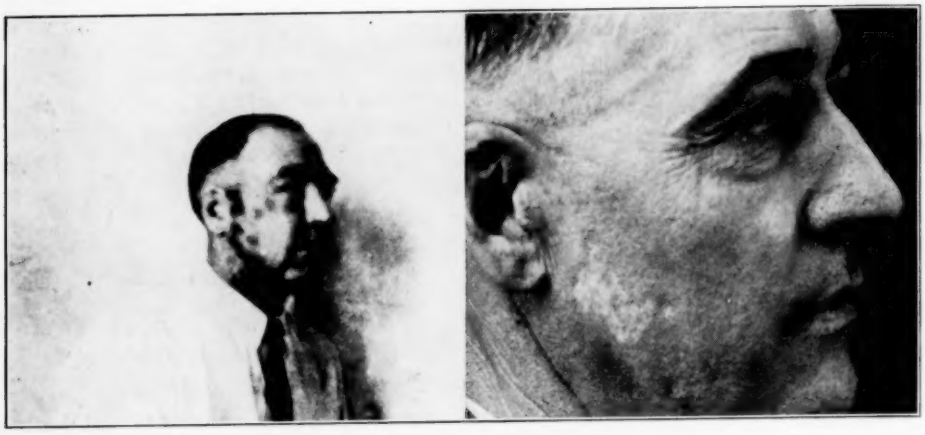

FIGURE 1.—Before and after treatment.

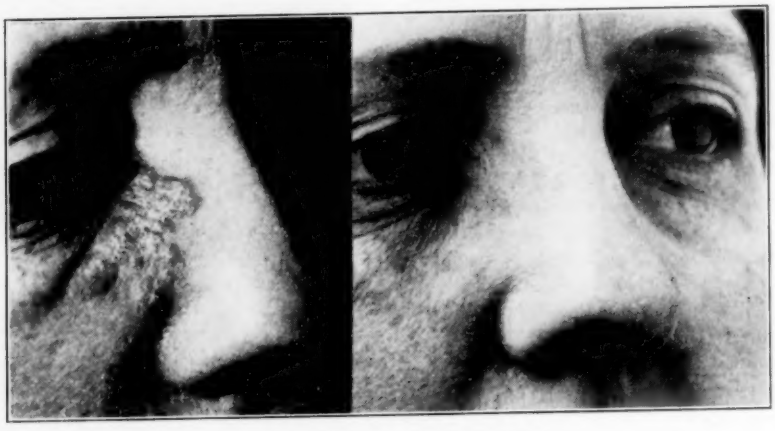

FIGURE 2.—Before and after treatment.

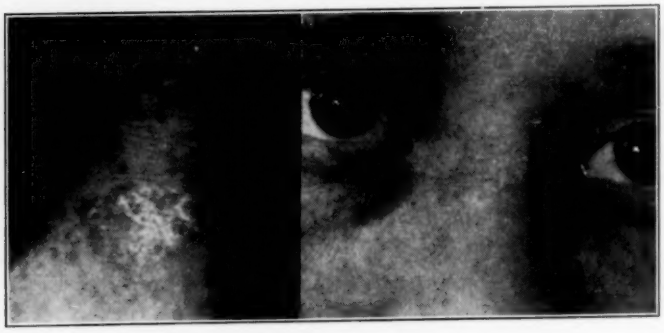

FIGURE 3.—Before and after treatment.

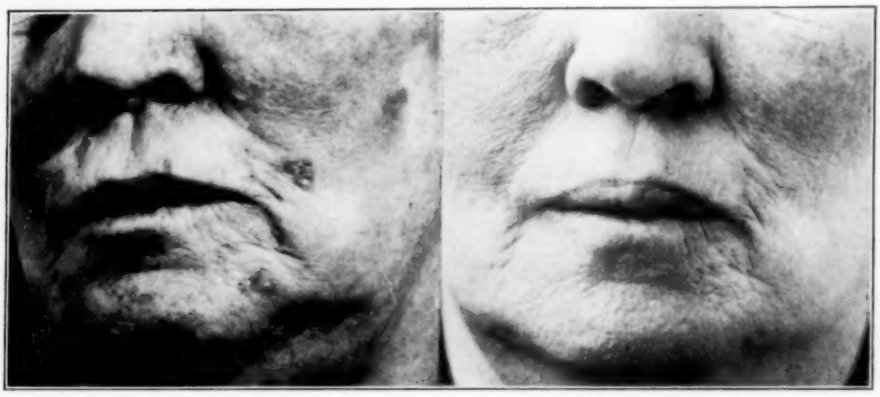

FIGURE 4.—Before and after treatment.

FIGURE 5.—Before and after treatment.

FIGURE 6.—Before and after treatment.

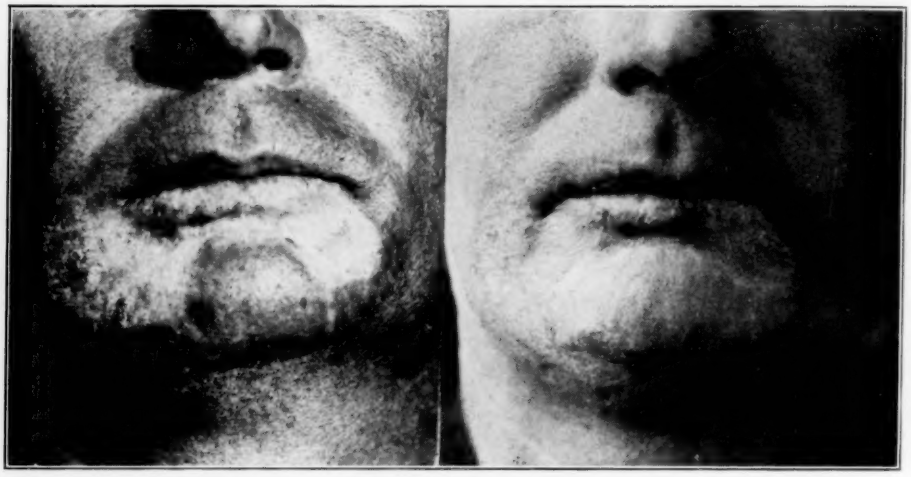

FIGURE 7.—Before and after treatment.

FIGURE 8.—Before and after treatment.

the fifth case in the entire series. It may be noted that the total dosage amounted to more than ten times that given in Case 1. In Case 3 a total of 1.0 gm. was given in twenty-seven injections. The injections were at first given once a week and later twice a week. The drug was well tolerated. In Case 4 a total of about 0.52 gm. in fourteen injections was given at intervals of from three to seven days without incident. In Case 6 a total of about 1.5 gm. in thirty-three injections was given at intervals of from one to two weeks without difficulty. In Case 7 a total of 1.4 gm. in thirty injections was given twice a week throughout the period of treatment without incident. In Case 8 a total of 1.0 gm. in twenty-five injections was given three times a week during the period of treatment without incident. These cases represent treatment schedules varying considerably in intensity according to the patient, total dosage and time interval; yet the results have been equally good and none of the patients showed sensitiveness.

Treatment in the Remaining Cases in the Series

One or two injections were given in three of the remaining twenty cases. The results in these are of no significance in establishing the therapeutic value of the drug. Two patients discontinued treatment for irrelevant personal reasons, and one showed marked hypersensitiveness to one minimal dose. In the latter case the lesions tended toward dissemination. In the remaining cases from five to thirty injections were given. The results in the eight cases reported individually may be rated as excellent, but in some of the remaining twenty cases the response was less satisfactory. I have, therefore, graded these twenty cases in four groups: (1) excellent, two cases; (2) good, five cases; (3) fair, seven cases, and (4) unsatisfactory, six cases. In all of the cases reported individually the results may be considered excellent.

In a consideration of the behavior of lupus erythematosus, particularly the peripheral spread and appearance of new lesions irrespective of the presenting lesions, it seemed desirable to consider only the results designated as excellent and good. In the six unsatisfactory cases are included the two in which one or two injections were given, and those in which there was intolerance to the drug. Obviously the results in this group must be placed on the debit side of the drug in an estimate of its therapeutic value, especially since patients were not treated if a pronounced tendency to dissemination was manifested, as it is well known that such patients are intolerant.

In the entire series of twenty-eight cases excellent results were obtained in ten (35 per cent) and good results in five (18 per cent). For practical purposes it may be said that fully satisfactory symptomatic results were obtained in about half the cases treated. These were, however, in a measure selected, as most cases with a tendency to dissemination were excluded. If all patients as they presented themselves had been treated with krysolgan, the results would not have been so satisfactory. Despite its disadvantages, krysolgan has probably afforded results that could not be duplicated by any other single therapeutic procedure except the use of other gold preparations.

Method of Administering Krysolgan

It is apparent that while krysolgan is a valuable therapeutic agent it cannot be considered specific for lupus erythematosus, and various methods of treatment will be necessary in the future as in the past. However, it may be possible, by careful attention to detail, to improve the results of krysolgan still further. In the series there were three cases intolerant to adequate dosage. In one only a single minimal dose could be given. In such a case manifestly no benefit will be obtained from the drug. In the second case eight, and in the third case sixteen, injections could be given. While in neither of these were the doses maximal, it is possible that small doses with long intervals might eventually have secured the desired result. In two cases fully adequate dosage was given (if one may judge from experience) without effect. In the

seven cases in which "fair" improvement was noted, the dose seemingly was adequate but more of the drug might have produced more improvement. Whether a time interval with a second course would show better results is not apparent from this series. It is possible that the individual dose as well as the total dose might have been materially increased advantageously in some of the cases. In that event, the dosage must have been strictly individual without a predetermined method of administration as individual variance in tolerance is pronounced. Further careful study of these points seems desirable.

Comment

Schamberg and Wright in a recent comprehensive article reviewed the literature with regard to the use of krysolgan in lupus erythematosus; I shall not, therefore, review it here. They used gold and sodium thiosulphate and obtained results similar to those obtained with krysolgan in my series, in about the same number of cases. I hope to be able to report such a comparison in my own experience in a future article, since gold and sodium thiosulphate is being used systematically at The Mayo Clinic. Krysolgan was first used in this series in September, 1926. Minimal doses at long intervals were given in the first six cases. After that the dosage was materially increased and the interval shortened without the occurrence of alarming symptoms. The patients who proved to be intolerant complained of general malaise with aching in the joints and a morbillous eruption. There was no evidence of true dissemination and the eruption involuted spontaneously after the drug was discontinued. One of the patients with an eruption of the chronic disseminate type returned a few months later because of an acute toxic syndrome, the result of acute lupus erythematosus. Sensitiveness varies enormously in different persons and treatment in a given case should be approached with great caution; however, large doses may sometimes be given advantageously. It would seem that the results obtained are reasonably permanent. In this series relapse did not occur in cases in which the response was satisfactory. More time must elapse before opinions on the permanency of results can be given. Some of the patients in this series have been well for about a year and a half. Krysolgan is evidently a remedy of real value in lupus erythematosus; in the chronic type at least it is probably superior to any single drug except some of the other gold preparations.

Summary and Conclusions

Doses of krysolgan varying considerably in amount and frequency have given satisfactory results in 50 per cent of twenty-eight cases of the chronic type of lupus erythematosus. These results could possibly be improved by careful attention to details as experience with the drug increases.

Patients vary enormously in sensitiveness to the drug but dangerous complications did not develop in this series. In three of the twenty-eight cases a morbillous eruption, general malaise, and pains in the joints developed but there was no evidence of true dissemination. As yet no decisive conclusion can be reached with regard to the permanency of the results.

The Physician's Dental Education*

By Willard J. Stone, M.D., *Pasadena, California*

A DISCUSSION of problems in which dentists and physicians are mutually interested can only be profitable if consideration is given to those features of their work which will make them more efficient advisors in matters of health. The public generally have advanced in matters of disease prevention quite as rapidly as the facts have been made available for them. Of all the means which have furthered the progress of medical and dental diagnosis the discovery of the X-ray by Roentgen in 1896 should take first place. The greatest advances in the clinical application of this discovery have occurred during the past fifteen years. The attention given by physicians to oral sepsis and its influence upon the health of the individual harboring it was negligible until about 1910 when Dr. Frank Billings published his articles upon focal infections. Since then physicians and dentists have found it necessary to coöperate in their work, to a degree not before considered necessary, in order to secure for their mutual patients the best results obtainable.

*Read before a joint meeting of the Pasadena District Dental Society and the Pasadena Branch of the Los Angeles County Medical Assoc., January 17, 1928.

I have been impressed for many years with the cursory attention paid by physicians generally to the condition of the mouths of their patients. If some lesion is present of which the patient complains the mouth will be examined, but even then with little understanding of the basic pathology which may be the cause of potential or latent disability. Many physicians are totally unable to distinguish pyorrhea even when it is very evident to the dentist. Physicians generally pay little attention to children's teeth beyond the teething period. Their recognition of the need of orthodontia is rather from the standpoint of aesthetics than from the need of the mechanics of the mouth. If a child is born with an evident deformity such as club-foot, the attempt will be made to correct it. An equally important deformity of the teeth will, perhaps in the majority of instances, go uncorrected. Much has been accomplished in the schools by medical and dental inspection, but the limitation of time, the lack of coöperation on the part of the parents, the failure to recognize the importance of the subject by those in authority, and the obstructive tactics of those who do not wish to acknowledge that certain things in nature may go astray, makes the problem a difficult one.

The Physician's Dental Education

Because of the growing appreciation and recognition that dentistry is an important branch of health service and cannot be ignored in the training of general practitioners of medicine, it will be of value to physicians interested in medical and dental education to study the Carnegie Foundation Report upon Dental Education in the United States and Canada, by Dr. William J. Gies, published in 1926.

I have endeavored to obtain data from leading medical schools regarding the amount of instruction given medical students in problems connected with dentistry since every practitioner of medicine should consider oral hygiene and oral disease as important problems in the care of patients. In reply to the inquiry the deans of seven of the leading schools of medicine in this country replied that no systematic instruction was given students of medicine in modern concepts of dentistry. In eight others of the leading medical schools, partial instruction was given either in the wards where the clinical clerks had access to the opinion of a supervising dentist or dental internes, or unorganized instruction was given in oral hygiene, prophylaxis and disease incidental to the general courses in medicine and surgery. At the University of Minnesota lectures in dentistry are given to senior medical students. At the University of Michigan the interpretation of dental films is taught as part of the course in roentgenology and instruction is given to senior students in oral hygiene. Washington University gives a required course in stomatology. At the University of Pittsburgh and at the University of Pennsylvania students are taught the interpretation of dental films and the importance of oral hygiene. Dr. Stengel believes that "the whole question of the importance of focal infections is sufficiently taught," or as he expresses it, "perhaps a little more than sufficiently."

The fact may be emphasized that such instruction as is given is adequate but that, with few exceptions, because of the overcrowded condition of the curricula in all modern schools of medicine, there has developed, of necessity, a restriction of special courses due to the lack of time. Of the seventy-nine medical schools in the United States only nine, in 1924-25, had required courses in oral hygiene, oral surgery or clinical dentistry in the undergraduate instruction. Many details of the specialties do not properly belong in the undergraduate medical course. With this point of view many educators, notably Dr. Emerson of the Indiana University School of Medicine, are in sympathy, while Dr. Edsall of Harvard has expressed the view that a great deal of the difficulty in medical education in recent decades has been due to the constant multiplication of special courses.

Each decade of experience in medical education, in an age of rapid advancement of knowledge, will serve to emphasize those features of instruction which are to be important to

the physician in the care of the sick. It has become necessary for the physician today, perhaps more than at any other period of medical history, to possess facts of practical value. While patients may be interested in a physician's academic propensities, they are much more concerned with his ability to adapt facts which may be of value to them. It has become a matter of what is relatively important and what is relatively unimportant for the physician to know since he cannot know all. The advance of knowledge has made it necessary for the physician to know something of the problem of dentistry in a definite way, for as the family advisor in matters of health he may be the first one to have opportunity to impart the facts.

The Carnegie Foundation survey is comprehensive and will do much for dental education in the future. One of the changes recommended has led to a course of five years consisting of two pre-professional years of college study and an undergraduate curriculum of three years to cover intensive training in oral medicine and clinical dentistry. This plan will leave for post-graduate instruction combined dental and medical courses for the training of specialists in oral surgery, for public health service and for research. Dr. Pritchett in his preface to the report, recognizes the difficulty of professional training and hopes that the problem may be solved in order that "the fruits of modern scientific health service may be within reach of that great majority of mankind that live upon modest incomes; for to train up a generation of physicians, of dentists, of nurses, whose service is so costly as to be out of reach of the self-respecting man of modest means who desires to pay his way, would be a dismal mistake in civilization." He does not venture suggestions as to how this desirable state of affairs may or will be brought about. It is apparent that if medical and dental curricula, as at present designed, could have adequately covered the ground of education in the essentials in a shorter period of years, educators would have recognized the fact. It has not been a question of how short a period of instruction the student needed but rather how long a period was necessary to furnish him the proper training. If prolonged training is necessary for physicians and dentists to do the right kind of work it is hoped that the public will find a way to meet the expense necessary for such labor as a health investment. The right kind of dental care can never be done upon the basis of quantity production. One great hope lies in the fact that education of the public as to the proper care of children's teeth will make unnecessary much of the extensive work now required in many adults since a large percentage of all cavities in teeth develop before the age of twenty-five years.

There is need for closer coöperation between dentist and physician, for as Dr. Gies has so aptly expressed it, "despite the prevailing medical lack of information regarding clinical dentistry many physicians, often against the dentists' protests, peremptorily order extraction of particular teeth, or sometimes of all remaining

teeth, on the assumption apparently that a dentist's judgment cannot be right when it conflicts with a physician's guess." He also mentions the fact that "the biological ignorance of many dentists owing to deficient education in the medical sciences and in the requirements of oral medicine, often accounts for the disrespect of physicians for the dentist's point of view and frequently makes dental consultations concerning the health of patients unreliable." The conclusions reached may be summarized as follows: "(1) Dentistry should no longer be ignored in medical schools; (2) The proper care of the mouth is as significant for the maintenance of health as any of the accredited specialties of medical practice; and (3) When dentistry becomes equivalent to an oral specialty of medicine it may be expected to bring many dental maladies into the realm of completely preventable disorders."

The prevention of disease and disability at all ages should become the predominating motive in the work of physicians and dentists.

Pyorrhea

Our understanding of the character of the progressive destructive process known as pyorrhea, as well as periapical lesions, has been much clarified during the past decade. So far as pyorrhea is concerned it seems that investigators have gone about as far as is necessary or expedient in the endeavor to find specific bacterial causes for the condition. So far as I am aware no definite organisms, vegetable or protozoan, may be held directly responsible for the condition in its incipiency. While the oral cavity always contains bacteria, most of the organisms which may be isolated from it are harmless saprophytes. Some varieties may undoubtedly become pathogenic under certain conditions. Sternberg discovered the diplococcus of pneumonia in healthy sputum.

A great many mouths harbor organisms which may be inert so far as their host is concerned. This carrier state may be a potential or actual source of danger depending upon a great many factors of immunity, specific as well as non-specific, the nature of which are unknown. That, however, the bacteria present in the mouth may be directly responsible for pyorrhea still requires proof. Indirectly as invaders of gum tissue surrounding healthy teeth bacteria probably play an important though secondary rôle. In a mouth neglected as to ordinary cleanlinesss in which caries and malocclusion with retention pockets exist, it is probable that tissue destruction is hastened by the bacteria present, but the primary cause lies in the lack of care and the mechanical features of malocclusion which make proper mastication difficult, if not impossible. Pyorrhea may be regarded as a slow progressive retrograde involvement of first the gingiva and later, during the course of years, the deeper tissues surrounding and supporting the teeth. The insidious nature of its progression may be taken as its most important characteristic.

In all essential tissues degenerative processes occur slowly with the course of years. Muscles become atrophic

or fibrotic from lack of proper use, the bones become decalcified, while the aorta and smaller arteries become sclerotic as a natural result of wear and tear favored many times by disease in other organs, or by abuse. From this standpoint the progressive lesions of pyorrhea may be looked upon as a degenerative condition rather than disease. Relatively few individuals beyond the fourth decade of life escape it. Relatively few physicians until a decade ago were interested in mouth sepsis. They preferred to leave the problem to the dentist, who many times failed either because of lack of knowledge, because of indifference, or through failure to impress upon the patient the importance of securing a clean mouth.

Periapical and Residual Infection

From every point of view it is desirable to possess a mouth free from pulpless teeth. For that large percentage of the population who have pulpless teeth with the corresponding tissue changes associated with them, the problem of treatment requires the best coöperation between dentist and physician. We may consider immediate and remote effects of acute or chronic periapical infection. In the acute abscess developing about the apex of a pulpless tooth with symptoms localized to the area involved, it is beyond the province of the physician to determine the most suitable local treatment advisable. Drainage alone may be the wisest procedure at this stage, but this the dentist must decide. For an acute abscess with focal symptoms, such as iritis, extraction may be the wisest procedure and the responsibility should be divided between the dentist and physician. Little difficulty is experienced as a rule in deciding the line of action in such cases for the pain may be acute and attention is focused upon its relief.

In chronic periapical infections it is safe to say that a very large majority may present no symptoms by which the attention of the patient is called to their presence. A large number of patients present themselves each year to physicians with the remote effects of such foci of infection. The physician depending upon his habit of thoroughness, or the lack of it, may fail to consider other foci of infection which such patients may harbour and without consultation with the dentist advise extraction, with the promise that arthritis or neuritis symptoms will be promptly relieved. Such advice may be detrimental to the patient as well as react against the physician. It is not within the physician's province to decide alone upon such matters. It is his duty to study so far as possible all foci of chronic infection which may be harmful to patients. This involves a consideration of the tonsils and sinuses, the digestive tract and its appendages, as well as the prostate, the seminal vesicles, the cervical canal, the middle ear, as well as such conditions as bronchiectasis, pyelitis or pyelonephrosis. The problem is a large one.

So far as the teeth are concerned physicians should realize that the dental roentgenogram does not tell all of the story. The mistake may be made in advising that pulpless teeth should be saved which do not show evidence of infection on the X-ray film. The work of Rosenow, Haden

and many others who have studied the problem should be carefully considered. The literature has grown enormously during the past decade. Price, Haden, Moody, Rickert, Beckwith, Simonton, Meisser, Gardner and others have added much to existing knowledge of the subject in the past few years. The following facts may be taken as established; (1) That the periapical tissues about teeth which give positive roentgenogram evidence of infection contain streptococci, usually of the non-hemolytic variety. The common varieties, by carbohydrate fermentation tests, have been found to belong to the groups known as mitis, fecalis and salivarius. Haden's recent work may be summarized as follows: cultures were taken from the apices and periapical tissues surrounding teeth removed "without contamination"; in one series of 500 pulpless teeth which gave radiographic evidence of infection. The percentage of positive cultures was 70.4% in glucose-brain-broth-agar, and 91% in glucose-brain broth. (2) Pulpless teeth which showed negative radiographic evidences of infection likewise gave a high percentage of positive cultures; i. e., in 600 such teeth the cultures were positive in 55.9% on glucose-brain-broth-agar and 83.8% in glucose brain-broth. Haden found streptococci only in 806 of 890 pulpless teeth (95.5%), while streptococci and staphylococci or staphylococci alone were found in 12 of 890 pulpless teeth. These findings are higher than those of Rickert who obtained positive cultures in 51% of 200 pulpless teeth. (3) From the experimental work of Rosenow, Haden and others, it has been shown that a variety of conditions have been produced in animals by cultures obtained from foci of infection about the teeth of patients. These conditions corresponded more or less accurately to the lesions present in the patients. Such selective localization has been repeatedly demonstrated for chronic arthritis, myositis, iritis, duodenal ulcer and pyelo-nephritis, less frequently encephalitis and thyroiditis have been produced. It may be mentioned that cultures from pulpless teeth, negative by roentgenogram, produced in 232 rabbits, a total of 168 lesions of joint, kidney, muscle, endocardium, myocardium, brain, eye, stomach and duodenum. The cultures obtained from pulpless teeth with positive roentgenogram evidence of infection produced in 224 animals a total of 181 lesions. (Haden)

Discussion

There has been a tendency to two extremes in the consideration of selective localization of infection from infected teeth. One group has believed that all foci of infection were inimical to health, while the other group has believed that the matter has not been proven because first, the methods used were not believed to be comparable to those which obtain in man and second, because some workers have failed to corroborate the work of Rosenow, Haden and Price. It must be acknowledged that some workers who have been adverse in their criticism, have not followed the original technic in their endeavor to prove the question of selective localization. Those physicians and dentists who believe the question still in

a debatable stage take the position, not without some logic, that bacteria such as streptococci exist in the tonsillar crypts as well as in the nasopharnyx and bronchial secretions of a large proportion of individuals, and yet such individuals may manifest no evidence of disease as a result of the presence of such bacteria.

The question cannot be decided quite so easily as this argument would imply. Periapical or residual infection exists as a more or less deeply entrenched focus in bone where adequate drainage is practically impossible. Some dentists have taken the position that, given evidence of such infection, there has been brought forth no proof that such foci are capable of producing systemic disease; in other words they believe that in many instances such foci are so-called sterile abscesses or are manifest evidences of healed bone changes. Such believers have deplored what they have termed unscientific proof founded upon speculation, and have continued to advocate retention of such teeth by any method of temporizing treatment which happened to be in vogue. I frequently see new dental appliances attached to teeth with obviously diseased roots and surrounded by pyorrheal abscesses, and not infrequently has expensive, extensive and tedious root canal filling been done in teeth with definite apical disease. Dentists who sanction such work justify their position because of the occasional rare instance, *from roentgengram evidence alone,* that healing of the diseased apical tissue may take place. Their attention should again be called to the fact that the percentage of positive cultures capable of producing definite pathologic lesions in animals, from pulpless teeth with negative roentgenographic evidence of infection, is nearly as high as that obtained by cultures from pulpless teeth with positive roentgenographic evidence of damage. It may be observed at this point that the conditions under which animals are injected intravenously with relatively large cultures of bacteria from infected teeth do not in all probability occur in man. Septicemia does occasionally occur from an area of infection about the teeth, but that it is a common occurrence must be doubted. The experimental side of focal infections about the teeth would be much clarified and the experimental workers would much more definitely establish their position, if they were able to produce in animals conditions similar to those which occur in man; that is, to embed their cultures in the animals teeth and demonstrate subsequently the pathological lesions found in man. It is possible that such proof may be obtained in the future.

There is reason to believe in the majority of cases that chronic foci of infection about the teeth produce their damage to health through slow absorption of toxins. In any large series of cases there will be a few in which the evidence may point to hematogenous transportation of the infection itself, but in the large majority the evidence points to slow absorption of toxins as the cause of certain symptoms such as myositis, neuritis or arthritis.

It may be appropriate at this point to quote from an address by Lewellys

F. Barker before the Maryland State Dental Association at its annual meeting in 1926. He stated (1) "that patients exhibiting various conditions (such as arthritis, myositis, neuritis, endocarditis, iritis, secondary anemias, etc.) do not always carry demonstrable primary foci of infection; (2) that when focal infections are present certain causal factors often coöperate with them in producing the conditions; and (3) that, owing to the lamentable tendency in this country to push ideas and practices to extremes there has, during the past five years especially, been clear evidence of over-emphasis upon the importance of focal infections as a cause of both local and general bodily disorders."

The position of the physician in the consideration of the conditions mentioned above is difficult, since in different individuals there may be different etiological factors. The patient with persistent myositis or neuritis may have periapical disease but he may likewise have a disturbance of metabolism with the retention of abnormal amounts of nitrogen products in his blood which in turn may be due to organic kidney disease or may be functional in the sense of faulty oxidation in an individual who exercises too little and whose intake of proteins is excessive, or again whose ability to utilize proteins may be lessened by hypothyroid activity. In those diseases which have a single etiological cause such as syphilis, typhoid fever, diphtheria, tuberculosis and scarlet fever, the clinical course follows a more or less orderly sequence. Complications which alter the regular course may be due to infections which while present in many individuals in health, are increased in virulence under certain conditions. Thus during the World War it was a common experience in the Base Hospitals to find that many soldiers were throat carriers of streptococci. No apparent harm came to many of them as a result of such carrier state. But when such individuals developed pneumococcus pneumonia they suffered from various complications such as empyema or otitis media which were due to the streptococcus infection they harbored in health. The streptococcus infection under such conditions became exalted in virulence during the course of the pneumonia. Cummings has recently studied the cause of death in small pox and concluded that "small pox is fatal only to throat carriers of hemolytic streptococci." It is apparent then that in the consideration of foci of infection within the body the physician must consider a large number of possibilities, some of which are known but many of which are unknown. It is necessary to consider the welfare of the patient as a whole, and to endeavor to do the most obvious things first. In chronic disabilities if the patient is able physically to undergo the ordeal, the physician should advise the extensive work many times necessary to render the mouth clean. This refers to the elimination of the diseased tissue and pyorrheal pockets by surgery in the hands of those of competent and extensive experience. I realize that I am treading upon somewhat dangerous ground since among the members of the dental pro-

fession there exists no unanimity of opinion on the subject.

I have followed the advocates of less radical methods in the treatment of pyorrhea for many years. There are many who believe that the teeth can be *cleaned* by so-called scaling methods. This I believe to be true, but I do not believe that pyorrheal pockets can be eliminated by any method short of surgical resection of the affected tissue. By this method reinfection of the pockets is prevented by the new tissue proliferation which occurs. Otherwise reinfection is inevitable. Such methods are available but are advocated by relatively few dentists largely, I believe, because they are unfamiliar with the results obtained by competent specialists in this field of work. It appears to me necessary to adopt radical means, if the measures may be called radical, to secure the desired end.

If the physician believes his patients' general health will be improved by extraction of pulpless teeth, he should endeavor to influence his patient to submit to such extraction, providing he may secure the assistance of a dental colleague who takes into account the subsequent mouth disability which may follow extraction, and its effect upon the general health of the patient including his digestive capabilities. On the whole nature displays wonderful adaptive capabilities. We are many times astonished at her many ways of compensation for defects. For example some patients for years will manifest no serious change in their general health who have been entirely without teeth and who have coincidentally had achylia.

There are certain risks entailed in any procedure, and it is necessary to consider whether it may not be safer not to disturb what may be a quiescent focal condition. This may be especially true in those who have evidences of extensive damage elsewhere, especially cardiovascular-renal disease. To expect any marked amelioration of symptoms or change in the function of organs the seat of degenerative processes is many times futile. It becomes for the dentist and physician alike in such cases a matter of doing as much as possible to restore adequate function. It may not be a matter of discretion to attempt more.

In the consideration of the extensive work many times necessary one can sympathize with both dentist and patient. Many may choose to take the position that part of a loaf is better than none at all, and are willing to temporize with any kind of work which is easily installed. Few individuals relatively are willing to undertake the expensive overhauling which their mouths demand from the standpoint of modern dentistry. Patients are many times compelled from economic reasons to secure work of a temporary but ultimately very expensive character. They have chosen amalgam fillings because of cheapness which may have been permissible providing the dentist had taken pains to explain that, because of the tendency to decay beneath such fillings within three years in a very high percentage of cases, such work was liable to prove more expensive in the long run.

It is probably true that prior to 1915 ninety percent of the dentistry done did not take into account care-

fully constructed restorations of carious teeth in the sense of their relation to the occlusal surfaces of adjacent or opponent teeth. This means that faulty dentistry before 1915 was responsible for much of the work which the dentist with modern training is endeavoring to correct.

Dental education will do much to remedy many of these conditions. Physicians of the coming generations will be given instruction in oral hygiene, more and more emphasis will be placed upon those factors which ultimately produce extensive damage such as malocclusion, more consideration will be given to inspection of teeth of school children, and more education will convince the large majority of intelligent people, that purely from the standpoint of prevention of subsequent trouble, it is necessary to secure competent advice early in life before extensive damage has been done. It would be a great step forward if dental dispensaries were available in each large community, founded upon adequate endowments by generously inclined people, where those who have an interest in health might secure a competent dental survey with advice covering their particular problems through the years to follow. The large life insurance companies could greatly assist in the matter of health education through publication of the facts. It would remain for those who believe to follow the advice given.

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Hypothyroidism*

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THE symptoms produced by excess of thyroid secretion or of aberrant thyroid secretion are so striking, and the explanations of the pathological-physiology have been so varied, that an enormous literature has accumulated dealing with hyperthyroidism. The opposite condition, lack of thyroid secretion (hypothyroidism), has been relatively neglected by the debaters and investigators. It is probably not because of the difference in the incidence of the two disorders of the gland, but rather that attention has been almost exclusively directed to the more obvious of the two and the one which actually is the more serious in its effects upon the life of the affected individual. Hyperthyroidism if left alone causes disability and often death. Hypothyroidism if left alone at the most causes disability only, but most often causes merely a marked slowing of the affected person's activities.

The thyroid gland is not absolutely necessary for life. It can be and has been removed with consequences serious enough to the individual, but not fatal. The hormone, now known universally as thyroxin, is absolutely necessary for normal cellular activity, for growth, for sexual and mental development. The action and interaction of thyroxin upon the other endocrine glands need not be gone into here. I take it for granted that these relationships are known to all. Our interest lies in the bizarre effects of an insufficient amount of thyroxin produced in the gland upon the bodily functions. Between the total lack of thyroxin and the normal amount lie a great number of states of lessened amount. Were this the only factor the problem would be fairly simple. It is complicated by the fact that every individual is different from every other individual, his response to irritants or to lack of any one important internal secretion is of different degree not only among individuals but in the same individual under varying conditions of nutrition, climate, infection, mental state, and what not. Consequently no mathematical measurement can correlate symptoms, no matter how accurate the instrument or apparatus may be.

For convenience of description hypothyroidism may be divided into three groups (1) Cretinism, (2) Myxedema of adults, (3) Masked or Occult Hypothyroidism. We are concerned here only with the last group. Theodore Kocher in 1909 was the first to call attention to slight forms of thyroid insufficiency. Previous to

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that time attention had been focused on cretinism and myxedema and the brilliant therapeutic results of Horsley and Murray. Apparently it was not thought that there might be symptoms resulting from continuous secretion of less than the normal amount of the thyroid hormone. Magnus-Levy in 1897 had found that there was decreased metabolism in severe hypothyroidism. Such estimations were only possible in well-equipped laboratories. To Benedict, du Bois and their associates we owe the practical application of the old cumbersome measurements of body metabolism. The development of the apparatus for measuring the basal metabolism has enabled us to pick out cases of masked hypothyroidism from other somewhat similar symptom groups. The condition is common. It occurs all over the world and is not confined to areas where goitre is endemic. However, in localities where simple goitre is common one would expect to find increased incidence of hypothyroidism in the adult population. No statistics are available yet on this question.

Endemic simple goitre is considered to be in itself an expression of a lack of some substance (iodin) which the gland must have in order for it to elaborate its hormone. If this substance is not supplied in sufficient quantity a lack of hormone results. Whether this lack will show in any particular individual later in life depends on his inherited constitution and upon various stresses and strains from his environment. If there is a lack of the thyroid hormone there is greater susceptibility to infections of various kinds, for the hormone has a decided influence upon bodily resistance and upon antibody production.

It behooves us, as doctors who are interested in restoring health to our patients, to pay more attention to the hypothyroid states.

I have taken from my records twenty-five consecutive cases, twenty one females and four males. This is about the usual proportion. The youngest was a girl twenty-one years old, the oldest a woman of fifty-six. Thirteen were over forty years.

Heredity—No data were obtainable concerning the influence of heredity. Barrett (1), among others, is convinced of the importance of heredity. He reports a remarkable family traced by him through six generations. Of sixty-one members hypothyroidism with dystrophies of the nails and hair were present in fourteen. There was also high frequency of feebleminded-ness and of neurological disorders of degenerate type. I have considered the following possibility. The Great Lakes region is known to be a locality in which simple goitre is common and where analyses of drinking water show almost total lack of iodin. The country was settled by people from the Atlantic Coast. After two or three generations with little or no iodin supplied in the diet, should it not be expected that the present generation would show more or less result of the lack of iodin and be otherwise well? Surveys show that from seventy-five to eighty-five per cent of young women have enlargements of the thyroid gland. This can only mean that iodin is lacking. Following pregnancies and other strains upon

the gland they arrive at middle life with so little thyroid hormone that it is not sufficient to carry them as normal people. I have no statistics to prove this hypothesis but am at present seeking to gather some. I present it as a working hypothesis to explain the frequency of the condition.

Etiology—It appears that not enough attention has been paid to injuries of the thyroid gland in infectious diseases (2). Attention was called by Kocher to mild states of hypothyroidism following severe general infections, typhoid fever, influenza, dysentery, furunculosis. Neither tuberculosis nor syphilis seems to play much part in producing hypothyroidism. Janney (3) feels that trauma and surgical operations are of little importance in etiology. The two periods of a woman's life, the beginning and cessation of menstruation, are important factors. Operations in which the ovaries are totally or almost totally removed also are influencing conditions.

Lawrence (4) studied twenty-five cases and found in 11 patients' minds the immediate cause was; 5 who said it followed pneumonia or severe influenza, 3 who attributed their trouble to pregnancy with toxemic symptoms, 2 thought that severe nervous and physical strain caused their trouble and 1 followed an operation for goitre. In only two of my cases was there a reasonably certain connection between infection and onset. One was a young man 22 years old who when 15 years old had severe influenza and pneumonia. The other was a young woman of the same age who when 16 years old had peritonitis following an operation.

Symptomatology—An unusually bizarre symptomatology is characteristic of this class of patients. Usually they are not ill. They go about their business, hold positions of more or less responsibility and often exhibit considerable energy. They come to the physician principally on account of an undue fatiguability. Even those with apparent energy do their daily tasks, then are so exhausted that they want to go to bed as soon as the evening meal is over. All writers have noted this as the most important single symptom. It was the chief symptom in 18 of my 25 cases and was present in all. "Tired out all the time," "Feel all in," "Can't go out to dances because I am so tired at night," are some of the expressions used. Constipation is common, a simple sluggishness of the bowels. McCarrison (5) has called attention to intestinal stasis in hypothyroidism. One of my patients retained a barium meal for 56 hours. This has been frequently noted by all writers and T. R. Brown (6) has again called particular attention to this condition in women over forty.

Headache and rheumatic pains were the chief complaints in four cases. We are so obsessed with the idea that focal infection is at the bottom of such cases that perfectly good teeth are extracted, perfectly innocuous tonsils removed, sinuses operated upon and drained, and appendices, even gall bladders, removed in the effort to relieve these people.

A colleague in the middle forties had had for several years repeated attacks of back and joint pain and stiffness often completely incapacitating him. He had noticed for several years past that he had difficulty in keeping his weight down and that he was losing his "pep," as he expressed it. He had had his tonsils removed, several teeth extracted and was about to have other "suspicious" teeth extracted when it was suggested that before he lost all his good teeth he might have a basal metabolism test made. Physical examination revealed no abnormalties and X-ray films of various joints and of the spine showed no lesions. His rate was minus 13 per cent. Not very low, one might say. However, as I believe that a small minus rate has a far greater significance than a moderate increased rate, I recommended that he take thyroid extract. He began with six grains daily. Within a week he was feeling much better. His stiffness disappeared. He has found that five grains daily is his dose. When he takes four grains for a few days his stiffness and pain return. When he takes six grains he finds he becomes a bit jumpy and sleeps badly.

Sundry aches and pains are complained of. Five patients had abdominal pain, the kind of pain which has been so often called chronic appendicitis, in general a meaningless diagnosis, and for which so many have been operated upon, gaining no relief whatever. One patient, a young woman, had cramp-like pains over the heart which disappeared rapidly in treatment.

Irregular menstruation was present in only two patients. One might expect more menstrual disturbances. In one case there was partial infantilism, a girl of 22 who had never menstruated and who looked and talked like a child of eleven years old. Two complained especially of drowsiness. It was hard to keep awake. One of these was a woman of 36 who was beginning to be myxedemic, the other was a slender man of 50, a priest.

Many complained of susceptibility to cold. No one complained of dry skin or of thinning of the hair or coarseness of the hair. These were occasionally elicited by questioning. Lawrence (7) notes this also. No one complained of the lack of perspiration on exertion although several admitted that that was true when they were asked about it.

Several complained that they had great difficulty in keeping their weight within reasonable bounds, others complained that however much they ate they could not put an ounce of weight on their spare frames. Hypothyroidism is certainly not a concomitant of excess weight any more than it is of under weight. This should be emphasized as the impression seems to be current that one does not find hypothyroidism in thin, underweight people. One of my patients definitely complained of losing weight.

Physical Signs—The general physical examination of these patients usually reveals very little. Some are overweight, some are underweight, some are normal weight. The thyroid gland may be visible as a swelling at the root of the neck or there may be

no evidence of the gland on inspection. So far as known there is no one type of bodily structure which seems particularly prone to develop lack of thyroid secretion.

The pulse rate and the blood pressure show no uniform decrease such as have been thought to be the case. In my series the lowest pulse rate was 56, the lowest blood pressure 90/70. The highest pulse rate was 104, the highest blood pressure 150/80. Higgins (8) says that the pulse may be accelerated, loss of weight occur and the condition not differ materially from the early active syndrome. Lawrence (9) says "A normal or accelerated pulse rate does not preclude a coexisting hypometabolism due to thyroid failure." Studying the effect of thyroid extract upon the heart he thinks that there are two effects, one is increase in work, the other is improvement in nutrition. The first often precedes the second by some time.

The blood shows no specific changes. Greene and the writer (10) reported upon a chlorotic type of anemia in young women with hypothyroidism. Mackenzie (11) reported secondary anemia and Stone (12) recently reported cases of myxedema which had masqueraded under the guise of pernicious anemia. Dock has also noted this type of anemia. There was no chlorotic type of anemia in the series here reported. Anemia was not the usual condition. When it occurred it was secondary anemia.

Kocher in his original description of the mild states of hypothyroidism bore heavily upon a relative lymphocytosis to substantiate the diagnosis. Even this is not always present. Lymphocyte cells, large and small, ranged from 47 per cent to 24 per cent. The former had B.M.R. of minus 19 per cent, the latter of minus 16 per cent. One patient, a woman of 34, 5 feet 7½ inches tall, weight 122½ pounds with a pulse of 68, blood pressure of 100/80 had 4,800,000 red cells, 95 per cent hemoglobin, 7000 white cells with 30 per cent of lymphocytes (24 per cent small, 6 per cent large). The basal metabolism was minus 22 per cent.

The basal metabolism rates in this series were between minus 12 per cent and minus 30 per cent. These estimations were all made with the Benedict-Roth machine using the graphic method and were made by the same person, a physician thoroughly acquainted with all the vagaries of making the readings. All patients were under standard basal conditions. Only those cases were taken whose metabolism was below minus 10. However, my conviction is that with symptoms such as have been described above even a consistent minus 8 per cent (allowing for errors which may creep in) may mean hypothyroidism. The significance of a small minus value is much greater than that of a moderate plus value. It is easy to overventilate and raise the consumption of oxygen with a corresponding increased metabolic rate. It is not easy, under the conditions of the test, for the patient to underventilate and produce a minus rate. Plus rates to me have no particular diagnostic meaning unless symptoms and physical signs agree with the reading. The minus reading, on the contrary, has

weight even though symptoms are indefinite and slight. Undoubtedly many patients live their lives through with a slight decrease in thyroid hormone and are never aware of the fact. Cushing (13) believes that many unrecognized hypopituitary cases are all around us. Some of these hypopituitary cases show a decreased metabolic rate. However, with the known interrelationship between the thyroid and the pituitary and the known influence upon cell metabolism of the thyroid hormone, it would be difficult to say whether such decreased metabolic rates were not due to the lack of thyroxin rather than to the lack of the hormone of the posterior pituitary lobe.

There is no relationship between the number or severity of the symptoms of which the patients complain and the depression of the metabolism. My experience coincides with that of Lawrence (14) who says that there is no relationship between the depressed metabolism and the amount of thyroid extract which will bring it to normal. Every case is a law unto itself and only experiment can fix the proper amount of thyroid extract required.

Lawrence (15) has found metabolic rates between minus 15 and minus 30 in cases of pathological fatigue (whatever that means), in cases of syphilis of the central nervous system, in cases of nitrogen starvation and in cases of hypofunction of the endocrine glands.

Diagnosis—It is not difficult to make the diagnosis of these cases if one is on the lookout for the condition and has the basal metabolism taken by a competent person. The methods of laboratory examinations in vogue now in so many places are not such as to inspire confidence in the results. Too many times the basal metabolism apparatus is turned over to a young woman technician who has learned to run the machine. Reports of plus 8 may well be actually minus 14 or less. With this comment in mind, the fact remains that the basal metabolism is the crucial test in the diagnosis.

In an otherwise rather normal looking person, a friend whom one sees frequently, complaints of being tired, of being a bit constipated, of having vague rheumatic pains or of vague abdominal pains do not necessarily suggest the possibility that he, or particularly she, may be one lacking in thyroid hormone. Yet such may be the case.

One must not be misled by the length of time the symptoms have been present. In Lawrence's (16) cases the average duration was 8 years. It was not possible to place the onset in all of my cases. One case followed measles and scarlet fever at the age of 8, twelve years before I saw her. One case seemed definitely to have followed a pregnancy 8 years before she came for examination on account of drowsiness, gain in weight, slight loss of memory but particularly because she became tired so easily.

A rapid pulse rate does not preclude hypothyroidism. All writers speak of this occasional paradox. Fever also may occur. Lee (17) has recorded a case with fever of weeks standing

from 99°-100° F, which had pulse rate of 50-66.

Differential Diagnosis—Many cases are called neurasthenia, nervous exhaustion, etc. I can recall vividly cases seen years ago where the most careful examination failed to discover any physical defect, which I feel now very probably were hypothyroids. Such a case as the following in the present series: a young woman art student, age 22, came complaining of being tired all the time. While she attended her classes and also taught, she had to drive herself, and by evening was utterly exhausted. She had been to a number of doctors, several of whom looking at her apparent health and well nourished body, scarcely examined her but told her she was nervous. She should go ahead and forget it. By the time she came to me she was disgusted with doctors but had consented to "go once more" as she said. She was averse to telling her symptoms as she had been laughed at frequently on account of the apparent triviality of them. A symptom which she had newly developed was a gripping pain in the upper left chest, so severe that when it came on she could scarcely breathe. In her past history there was dilatation and curettement of the cervix for vaginal discharge when she was fourteen years old. An appendix operation followed by prolonged infection, ventral hernia and repair of hernia at 18 years. Also she said that she gained weight so quickly that she had almost to starve herself in order not to grow enormous. Physical examination revealed no organic lesions. The thyroid region seemed a little full but there was considerable fatty tissue in the skin. The B.M.R. was minus 16. She was given thyroid extract. The next B.M.R. eight weeks later was zero and she was feeling quite well, not only able to work without fatigue but she could eat without gaining weight rapidly.

There are cases which for want of a better diagnosis one has called gastro-intestinal intoxication or even migraine. In 1922 a thin woman, small boned, and of small frame, then forty-one years old, complained of recurring attacks of headaches and nausea. Her father suffered from headaches all his life. He died at 86 years old, the cause not known. One sister has headaches and one brother had pulmonary tuberculosis. When twenty-eight years old she weighed 135 pounds. About that time she had an attack of jaundice followed by stomach trouble. She has never been well since. Her weight gradually was reduced to 109 pounds, she was constipated and had frequent headaches oftentimes with neusea and vomiting. The most careful physical examination including gastro-intestinal X-ray examination failed to show any lesions. There was general abdominal soreness on palpation, a sign the significance of which was not appreciated at that time. She was given general supportive treatment, gained four pounds in three months but was not much improved. She was next seen in February 1926 in about the same condition. She was quite constipated and the skin had a muddy, somewhat yellowish tint. No gall bladder or liver disease

could be demonstrated. When she was next seen in April 1928 she had the same series of symptoms. This time the diagnosis of hypothyroidism was made and she was given a B.M.R. test. It was minus 20. Thyroid extract was given. At present writing she is better, has gained weight and her bowels move more normally.

General soreness in the abdomen on palpation, particularly in the appendix region, is frequently found. Chronic appendicitis has been a diagnosis often made and many a normal appendix has been removed without benefiting the patient. In the common acceptance of the term I do not believe there is such a disease. Subacute and recurrent appendicitis is a definite entity and operation is a curative procedure. But that an appendix should become chronically diseased and give indefinite symptoms without previous acute attack is, I believe, a rare occurrence. The art student reported above had "chronic appendicitis," was operated upon and then developed peritonitis and later ventral hernia. This was in my opinion an unjustifiable operation.

Others as well as I (18) have reported upon the vague gastro-intestinal symptoms of occult and early tuberculosis of the lungs. Such cases have been operated upon both for "chronic appendicitis" and for gastric ulcer.

Occult tuberculosis can readily be confused with hypothyroidism in the underweight individual. I am sure now that I have made this error in the past. The symptoms are practically identical. The chief symptom is undue fatiguability and a train of symptoms which are called neurasthenic. The basal metabolic rate settles the diagnosis, for in afebrile tuberculosis unless the patient is markedly undernourished the B.M.R. is normal (19). The following case I feel sure I should have diagnosed occult tuberculosis several years ago.

A priest aged 49 said that up to two years ago he had never been ill. He fell on the ice at that time striking his back, and since he had not been altogether well. He is tired all the time and has a tendency to fall asleep as soon as he eats his evening meal. He has not lost weight, has a good appetite, but is constipated. There has been some difficulty in starting his urine. A year ago he had his prostate massaged. There was no cough or shortness of breath. On examination he was a fairly well nourished man, 5 feet 6 inches, weight 142 pounds. There was slight impairment of the percussion note at the right apex posteriorly. The breath sounds were harsh, but no râles were heard. The lungs were elsewhere clear. The heart was normal. The pulse rate lying down was 80, the blood pressure 120/80. Nothing abnormal was felt in the abdomen. The reflexes were present. The blood showed no abnormalities. The prostate gland was enlarged and soft. The urine was normal.

Fluoroscopic examination of the chest showed slightly hazy apices, both lighting up on cough, greatly enlarged hilum shadows with heavy streaking in the inner zones in the 1st and 2nd interspaces on both sides. The right diaphragm was slightly tented at its middle portion. The heart shadow

was normal. Intradermal O.T. 1/10 mg. was strongly positive in 24 hours. The basal metabolic rate was minus 17 per cent.

Treatment—Either thyroxin or thyroid extract can be given. The former given intravenously may be used where one wishes a rapid effect. However, I have not found it necessary to use thyroxin and prefer the tablets of thyroid extract given by mouth. Dosage varies widely. Some patients have taken fifteen grains daily. Six to nine grains daily is an average dose. There is no relationship between the depression of basal metabolism and the amount of thyroid which will normalize the patient. Lawrence (20) says that in thyroid deficiency thyroid extract tends to normalize functions, to bring low pressure up and high pressure down and can benefit symptoms only in so far as it can normalize the nutritional level of the body.

In one of his papers he draws one conclusion which cannot be too strongly emphasized. He says "thyroid extract in non-toxic amounts has no specific action in reducing body weight, except as it dissipates myxedemic deposits and causes the elimination of abnormal accumulations of fluid. By its effect on nutrition it frequently causes a gain in weight as basal metabolism becomes normal. Progressive loss of body weight as a result of its administration is, as a rule, a toxic effect. Its use as an aid in reducing weight in patients with normal thyroid function is therefore illogical, and either inefficient or dangerous."

Summary

Hypothyroid states are common and often are unrecognized for years. The affected persons in the meantime have a bizarre group of complaints the chief of which are (1) a sensation of being always tired, (2) constipation, (3) susceptibility to cold, (4) various aches and pains, (5) in women, amenorrhea or menorrhagia.

Physical signs are singularly lacking. Both overweight and underweight are found. General abdominal soreness, often greatest in the right iliac fossa, is frequent. A carefully measured basal metabolic rate reveals depression in all cases. This is the necessary criterion for diagnosis.

Differential diagnosis must be made from (1) the neurasthenic syndrome, (2) so-called "chronic appendicitis," (3) migrainous headaches, (4) rheumatic aches and pains now so widely believed to be due and often are due, to focal infection, (5) occult tuberculosis, (6) diabetes, (7) pernicious anemia, etc.

Thyroid extract can only normalize the nutritional needs of the body and should never be administered to reduce weight in individuals with normal thyroid function.

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The Causes of Flatulence

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THE symptom, flatulence, indicates the presence of excess gas in the bowel, or the passage of gas from the rectum in noticeable quantities. The causes are so numerous that flatulence is in itself of little diagnostic importance, but occasionally it is the chief or only symptom, or the earliest noticeable symptom, and then its study becomes of value.

From a circumspective point of view gas gets into the bowel in three ways. It may be *swallowed,* may be *generated* in the alimentary tract, or may be *excreted* through the bowel wall into the lumen.

Outline of Causes

Swallowed Gas
- in the form of gaseous foods
- because of frequent swallowing
  - on an emotional basis
  - with lachrymation in eye diseases
  - with nasal disease
  - with pharyngeal disease
  - with oral disease
  - with esophageal disease
  - from chemical irritation
  - from mechanical irritation
- because of excessive motility of the alimentary tract
- because of decreased absorption in the alimentary tract

Gas generated in the alimentary tract
- from diseased bowel wall
- from foods
  - because of the inherent food qualities
  - because of faulty digestive juices
  - because of poor absorptive capacity
  - because of too rapid passage of food
    - through the small intestine
    - through the large intestine
  - because of delayed passage
    - through the small intestine
    - through the large intestine

Gas excreted from the blood into the bowel lumen
- because of saturation of the blood
  - from inhalation of gases
  - from extensive diseased regions in the body
  - from improperly functioning excretory organs
    - vicariously in extensive lung lesions
    - vicariously with severe liver lesions
    - vicariously in advanced renal lesions

Swallowed Gas

Gas is swallowed with every bit of food or liquid that passes down the esophagus, but ordinarily it is in small quantities except perhaps when large amounts of gaseous drinks such as charged water are imbibed. It is removed by chemical action in the bowel lumen, or by absorption into the blood stream. Nitrogen is chemicophysically somewhat inert, and while a portion is undoubtedly absorbed, when ingested in sufficient quantities some may pass on through and become flatus. However, in a healthy individual the probability of flatulence from swallowed air is remote.

Air swallowers as a rule are *not* healthy individuals. There may be a nervous basis for the habit, such as some emotional state. The concommitant flatulence is due not so much to the excess air swallowed as to gas accumulating in the large bowel because of generally increased activity of the autonomic nervous system. In emotional people food is hurried through the stomach and small intestine before digestion is complete, and the undigested unabsorbed food is broken down by colonic bacteria with the generation of gas. The gas is frequently expelled because of restlessness of the large bowel. This will be discussed in detail later.

Air swallowing is apt to occur with focal disease of the upper respiratory and alimentary passages. The irritation produced by pressure from an esophageal diverticulum, an aneurysm, goitre or enlarged thymus may cause it. A small esophageal ulcer or erosion, or beginning carcinoma can make the patient swallow more than usual. The irritation may be from retropharyngeal tuberculous processes, or from neoplasms at the vocal cords, or tuberculous and luetic granulomata and ulcers. An excessively long uvula, very large or infected faucial tonsils, or pharyngeal adenoids may lead to air swallowing. A common cause is chronic catarrhal of the nasopharynx and accessory sinuses. The persistent mucoid discharge running down the posterior wall of the pharynx induces repeated swallowing efforts. The mucous membrane is irritated in pharyngitis siccum. Eye diseases with lachrymation may cause increased swallowing of fluids passing through the lachrymonasal ducts. Oronasal deformities predispose to air swallowing. Any chronic oral irritation may lead to salivation and when the saliva is swallowed excess air is introduced. Oral irritation may be from diseased gums, teeth or mucous membrane; from tobacco, chewing gum or toothpicks; or indirectly from the use of mercury and iodides internally. Irritating gases have a tendency to cause air swallowing through the induced rhinorrhoea and choking that occur at times. During hay-fever season susceptible individuals may swallow the profuse oronasal secretions and take in enough air to cause flatulence.

Now the activity of the entire alimentary canal is affected by lesions at any point between the mouth and the anus. Carious teeth may lead to increased intestinal motility. Undigested food thus reaches the large bowel where gas is generated. When such a condition exists, not only is the gas volume increased by excessive air swallowing as described above, but the gases which entered the stomach with the food are hurried through into the colon before they can be disposed of by intestinal absorption. Thus gases swallowed in ordinary quantities may lead to flatulence when local alimentary lesions exist.

This brings us to the second and largest division. Gas may not be swallowed as such in the food, but may be generated within the lumen of the alimentary tract.

Gas Generated in the Bowel

Some gas is customarily present in the large bowel after a night's undis-

turbed sleep, generated by the action of colonic bacteria on food remnants in the caecum. This may be passed at stool. The longer food remains subject to the action of intestinal bacteria, the more gas there is formed, hence flatulence may be noticeable after going awhile without the customary bowel movement. Much of the colonic gas is absorbed through the healthy bowel wall, into the blood stream, and done away with by means of chemical reaction or excretion through the lungs. A constipated individual may have a disagreeable breath from intestinal gases.

Gas generated in the lumen of the alimentary tract comes only from food or from necrotic bowel lining. The commonest cause of flatulence lies in the fermentation or putrefaction of material that has been ingested.

Normally, ordinary articles of diet such as cooked potatoes and tender meat are acted upon by juices in the stomach and small intestines, spend a sufficient amount of time here for proper digestion, and after about two hours the remaining material that has not been absorbed gets into the caecum. Here, in liquid state, further absorption occurs and the cellulose-covered starch granules that escaped in the upper intestine are broken down by colonic bacteria. If for any reason *food is hurried through the small intestine,* much undigested material reaches the caecum. Likewise, if there is *deficiency of alimentary juices* any place along the way, certain food elements reach the caecum undigested and become suitable pabulum for bacteria. Thirdly, if *obstruction* occurs at any place in the intestinal tract, the food elements in the bowel lumen at the time become subject to bacterial decomposition: and with the impoverished circulation which necessarily accompanies such stasis there is deficient secretion of digestive juices and deficient absorption of digested material.

Certain foods resist the digestive action of the gastric and duodenal juices, but are readily broken down by bacteria that normally inhabit the colon, with the liberation of gas. Dried beans and the coarse vegetables are examples. The starch granules of dried beans have thick coverings which are acted upon only slowly by succus entericus. The excess cellulose in lettuce, celery, cabbage, radishes and spinach leads to colonic fermentation. Gases generated from such foods usually have a penetrating but not foul odor, and consist mainly of acetic acid gases and carbondioxide.

Certain materials exert a chemical irritative effect on the bowels. These may be ingested, or may be excreted directly into the bowel lumen through the bowel wall, from the blood stream.

Poisons that reach the bowel lumen by way of the blood stream may have been inhaled in the form of noxious gases, or generated in the body itself. In nephritis poisons are vicariously excreted through the bowel. In diabetes and cancer, chemical irritants may gain access to the bowel from the blood stream, and in many high-grade infections and toxemias such a situation frequently exists.

The commonest manner in which chemical irritants are applied to the alimentary tract, however, causing

rapid peristalsis so that undigested food is hurried into the colon is by oral ingestion of irritating substances. These may be in the form of drugs known as cathartics. Many cathartics, as rheum, have been prepared from articles of diet. Castor oil is expressed from the castor bean which is used for food in parts of the world where it is grown. Some cathartics are made from wild apples, and the ordinary commercial "eating apple" has a more or less pronounced chemical irritant action in the alimentary tract. The internes at Presbyterian Hospital used to call applesauce "Dr. Sippy's cathartic."

Foods in particular that cause rapid passage of material through the small intestine are cabbage which is also as before mentioned a resistant article of diet: preserves whose irritative action is partly due to complex carbohydrates; maple syrup and honey which contain carbohydrates that are not only active chemical irritants but are also poorly hydrolyzed by succus entericus. Some of these complex carbohydrates reach the colon where bacteria act upon them liberating more gas. Poison meats are so strongly irritating that a distinct inflammatory reaction or enteritis is frequently produced. Decomposed foods in general have a similar action, and the so-called ptomaines are responsible for much of this chemical irritation.

The foods just mentioned also frequently irritate the large bowel. The gas generated in the colon becomes an irritant in itself, and flatus is passed.

Agar and mineral oil, considered harmless inert laxatives, may be present in such large quantities in the bowel lumen and so thoroughly coat small food particles as to interfere with digestion. The undigested bits reach the caecum where bacterial action yields gas.

The small intestine may be irritated with resulting increased peristalsis from focal lesions of the stomach, duodenum and ileum. Ulcer of the stomach is frequently accompanied by increased peristalsis, and the symptoms presented may be wholly those of a bowel disturbance, and not in any way specific to gastric ulcer. Duodenal ulcer and pyloric carcinoma may have a similar effect. Catarrhal inflammation of the upper part of the small intestine may lead to excessive peristalsis. Flatulence has occurred with extensive burns, poisoning by mercury, and in purpura. Benign tumors such as melanoma, angioma and the pedunculated lipomata that occur in elderly individuals may lead to flatulence in similar manner. Duodenal diverticuli may cause excessive peristalsis, as may also herniae at the ligament of Treitz, ptosis and kinks. The duodenum may be compressed sufficiently, at the point where the superior mesenteric vessels course over it, to lead to irritation and increased small bowel peristalsis. A not at all infrequent cause of flatulence is some lesion of the gallbladder or ducts such as stones, chronic inflammation or cancer. In a similar manner pancreatic cysts, stones and tumors may cause increased small intestinal peristalsis. Pressure applied to the bowel any place from the cardia to the anus may be sufficient cause for aggravated movements. This pres-

sure may be from growing tumors such as retroperitoneal sarcoma or hypernephroma: from benign and malignant neoplasms of the ovary or uterus; from a gravid uterus; from a distended bladder; or from large hydatid liver cysts. Abdominal aneurysm may exert sufficient pressure to bring about increased intestinal peristalsis.

Where increased intestinal motility is associated with abdominal swellings, not only local pressure against the intestine but also local circulatory disturbances that have been induced must be taken into account. When the abdominal circulation is embarrassed in any manner, both secretion and absorption suffer. With faulty secretion of digestive juices, food particles escape to become pabulum for colonic bacteria, and decreased absorption also permits food to reach the caecum. There are many causes of embarrassed circulation, both general and local. A general impoverished circulation may depend upon heart lesions with which high blood pressure is frequently associated. It may depend upon obstruction in the lesser circulation through the lungs from fibrous tissue, fluid in the pleural cavity, collapse of the lung, solidification or cancer. Portal obstruction accompanying cirrhosis of the liver may lead to damming back of venous blood in the mesenteric vessels with consequent poor nutrition of the bowel walls, and diminished or faulty secretion, absorption and motility. Obstruction of the portal vein by pressure from a growing tumor, or thrombosis, or mesenteric arterial embolism or sclerosis are examples of locally impoverished circulation.

Another cause of flatulence, following in sequence that just described, is the defective secretion of alimentary juices. Normal secretions from healthy alimentary glands digest food, inhibit bacteria, and apparently neutralize toxins. From the gastric mucosa come pepsin and chemicals that give rise to hydrochloric acid. These digest fibrin, hydrolyze polysaccharides, and inhibit bacterial growth. In the duodenum is succus entericus with protein-splitting and fat—and sugar digesting material from the pancreas and biliary passages. If there is deficiency of hydrochloric acid (achlorhydria) certain bacteria are permitted to enter the intestine noninhibited where their activity may give rise to gas. Certain polysaccharides and fibrin are not digested in achylia. Thus in chronic high-grade anemia, cancer of the stomach and debilitating diseases with which this is characteristically associated, undigested food elements gain access to the large intestine. Here protein materials are broken down with the liberation of foul alkaline gases; fats yield acetic, butyric and similar acids and gases; and carbohydrates acetic acid and carbondioxide. Fats escape biliary digestion when the ducts are obstructed or there is dearth of liver parenchyma. Ordinary proteins such as muscle fibers escape digestion when there is obstruction to the pancreatic ducts as in cysts, cancer of the head, and stones.

The intestinal flora as a rule depends upon the type of food available. Acid-withstanding organisms are in the milk-fed infant's colon. Large numbers of B. Welchii infest the colon of those suffering from achylia. With but few exceptions, the colonic bac-

teria themselves are not responsible for excess flatus. Their continued existence is dependent upon the pabulum and the state of health of the intestinal walls.

The walls of the large bowel may undergo changes which lead to the production or passage of excess gas. Here again, there may be *poor absorption* of gases because of the injured lining or chronic congestion. *Too rapid passage* of gases to the exterior may result from increased peristalsis. It is possible, also, that disease of the colonic glands with *defective secretion* may permit excessive generation of gas.

Diseâses of the colonic wall itself that lead to flatulence are carcinoma, strictures and ulceration. Ulceration is due to tuberculosis, syphilis, amoeba, and possibly diplobacilli. There are several systemic conditions such as deficiency diseases, nephritis and diabetes in which so-called "nonspecific ulceration" of the large bowel occurs.

Diverticuli and benign tumors may be sources of irritation and gas normally absorbed in the caecum may be passed. In tuberculosis of the peritoneum covering the colon or of the colonic lining, decreased intestinal motility usually occurs. This also happens with syphilitic and carcinomatous ulceration, and stools are retained with generation of excess gas. There are certain cathartics whose action is chiefly on the large intestine. Phenolphthalein is one of these. The resulting flatulence is due to excess motility.

Gas may be poorly absorbed from the large bowel because of impoverished blood supply, especially when pelvic lesions lead to local congestion. Undoubtedly more than one factor is concerned here, for when pelvic inflammation exists there is irritation of the adjacent bowel wall, reflex nervous disturbances in the colon, and chronic active congestion. Malposition of the uterus may lead to flatulence.

Paralysis of the large intestine may cause flatulence. The causes of paralysis are numerous. Some have already been named; local bowel lesions such as appendicitis, tumors and ulcerations. Peritonitis—either suppurative, tuberculous, or carcinomatous—eventually leads to paralysis.

A great many lesions of the central nervous system may be responsible for flatulence. Transverse myelitis, spina bifida, hematoma and the granulomata which produce local pressure against the spinal cord may cause lessened colonic motility. The spinal cord may be compressed by accidental dislocation or fracture of a vertebra, by caries or osteomalacia. Metastatic tumors to the vertebrae notably from the breast and prostate gland may press upon the spinal cord leading indirectly to slowed peristalisis and flatulence. Syringomyelia and multiple sclerosis should be mentioned.

Interference in the reflex segmental arc may lead to lessened movement of the intestine. This occurs in tabes, anterior or posterior poliomyelitis, and peripheral neuritis. Encephalitis and meningitis may lessen large intestinal motility, and cord changes are frequent in diabetes and pernicious anemia.

An irritative nervous influence may be exercised upon the intestine. Men-

tion was made of this when discussing the air-swallowing habit. Emotional states frequently lead to flatulence, undoubtedly through activity of the automatic system. Since the autonomic system is intimately connected with the endocrine system, flatulence can occur during the adjustment periods of life in adolescence, the catamenia, pregnancy and the menopause; with diseases of the thyroid, suprarenal and pituitary glands. Insanity from syphilitic paresis, senility or dementia praecox may be accompanied by flatulence due indirectly to nervous disturbances.

Splanchnic congestion occurs in vagotonia. There is frequently reflex spasticity of the large bowel with sexual excitement.

Gas Excreted From the Blood

One more group of cases of flatulence should be mentioned, that in which there is vicarious excretion of gases through the intestinal wall. After ether anesthesia the flatus passed may be ethereal. Ordinarily the lungs excrete gases, but when these organs are extensively destroyed or damaged as in pneumonia, cavitation or collapse, gases may be excreted through the colon. When the body is saturated with gas, excretion is partially by way of the bowel but most of the gas passes out through the lungs. Foul gas may be eliminated vicariously when the body is saturated by absorption from some extensive gangrenous region. In gangrene of the lungs there is saturation with gases and damaged pulmonary tissue. If the bowel wall is relatively intact much of the poison gas may be excreted through it. Vicarious elimination possibly also occurs with severe hepatic lesions and in advanced renal disease.

It would seem in this outline that there is repetition, but many of the causes of flatulence overlap. It emphasizes the fact that flatulence and its individual causes is by no means a simple condition.

Diagnosis and Treatment of the Anemias*

By W. W. Duke, M.D., *Kansas City, Missouri*

OUR knowledge of the diagnosis and treatment of anemia has developed to a large and important extent during the past two decades. The treatment of anemia has been dealt with so completely in recent literature that I shall discuss in this paper chiefly the diagnosis of anemia.

The diagnosis of anemia in a marked case is so apparent that one may be surprised that I should care to discuss the topic at any length. The fact is, however, that in the milder cases of anemia the diagnosis may be beset with difficulties and give rise to clinical pictures which are most perplexing. Even in what might be called mild cases of anemia, the patient may be wrecked with a cord lesion, multiple neuritis, mental deterioration, and other complications which mask completely the symptoms of the anemia itself and which often lead to error in diagnosis. In fact, it is common in cases of this sort for the anemia to be overlooked entirely even by careful internists.

In the early days of medicine, physicians were accustomed to diagnose anemia on the basis of the changed color, that is by observing pallor of the skin and membranes. With the development of laboratory methods, this simple direct method of examination has been sadly neglected. This is unfortunate because laboratory methods at best are not at the disposal of all physicians and more unfortunate still, they frequently mislead the physician using them to such an extent that he may not discover the actual status of affairs. Red counts, hemoglobin estimations, and examination of the cells of the blood have been used extensively for many years. More recently, Rowntree and his associates have given us a method for estimating blood volume which they believe is accurate and simple enough for clinical purposes and which they believe should add to the accuracy of laboratory methods in gaining an idea concerning the status of the blood. Unfortunately, our old idea that red counts and hemoglobin estimations tell the whole story concerning the status of the blood is not correct. A person with a normal red count and hemoglobin per cent may be either anemic or plethoric due to an increased or reduced blood volume.

Rowntree and Brown's studies, while interesting from a standpoint of actual blood volume, do not give us an absolutely dependable means of

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determining whether or not the volume of blood found in a given case is optimum for the patient under observation or too large or too small. This, theoretically, cannot be determined with accuracy by measurements of height and weight, for as is apparent, an athlete of a given height and weight needs a greater blood volume under normal conditions than a flat phlegmatic individual, such as a case of hypopituitary obesity. This apparent fact hardly needs discussion. Muscle tissues not only contain more blood than fat, but a muscular individual has larger internal organs than a fat individual. The heart, large vessels, the liver, and the spleen, etc., which contain enormous quantities of blood should give rise to a disproportion in blood volume between muscular and fat individuals which could hardly be estimated theoretically by measuring height and weight.

We are confronted with still greater difficulties when we try to determine whether a given blood volume is optimum for a patient who has a pathologically increased cardio-vascular space which must be filled and which therefore, demands a greater blood volume for the optimum per unit of weight than would exist in patients who might not have such an anomaly. For example, a patient with a largely dilated heart or an aneurism, or enormous varicose veins, should have, to be optimum, a larger blood volume than a patient who has a normal sized heart and vessels. Furthermore, in patients whose weight is pathologically increased as we observe in patients with osteoplastic tumors, the blood volume to be optimum should be smaller per unit of weight than it is in patients who do not have osteoplastic tumors.

In pernicious anemia, we have an anomaly which leads us still further astray. A number of years ago, Dr. D. D. Stofer and I (1) found that in this disease makrocytes tend to lodge in the capillaries and give rise to a large disproportion between the capillary blood count and the venous blood count. In fact, in an untreated case of pernicious anemia, the capillary count is usually 25% to 50% or more higher than the venous count. This disproportion, we found to be constant regardless of whether the patient had been transfused and had a reasonably high count, or if untreated and had a very low count. Since the introduction of the Minot-Murphy Diet, we find that the two counts in treated cases tend to come closer together, and as the count nears four million, they may be approximately the same.

We must frankly admit, therefore, that in our study of anemia, we are up against variables which are discouragingly gross. This led me many years ago to try to devise a method for studying color which might overcome some of these difficulties. I have described this method in detail in previous papers (2) and need only mention it briefly in this connection.

As previously mentioned, it has been a time honored custom for physicians to decide whether or not a patient is anemic or plethoric by observing his color. Methods of examination for this purpose have not been satisfactory because of the fact that some individuals who are normal have red

faces, and some pale faces. Each may be normal so far as the status of the blood is concerned. The face as an organ of expression varies in color on this account. This is true also of the lips and nails. Furthermore, the skin varies enormously in color because of its important function in the regulating of loss of body heat. When it is urgent that the loss of heat be increased, the skin vessels are likely to dilate, whereas, when it is urgent to retain heat, the reverse status obtains and gives rise to a pale skin. The conjunctiva is not a good place for the observation of color for this change in color with posture. If a person is sitting, a column of blood under negative pressure tends to make the conjunctiva pale. Whereas, if the person is lying down, especially if the head is lower than the heart, the same capillaries tend to be abnormally full because of the effect of gravity. This change in color is quite marked. One can convince himself of this fact if he will compare the color of his two hands, one which has been held above the heart for a few moments and the other below.

There is one skin area in which color varies remarkably little under the usual conditions under which the physician sees a patient, in house, office, or hospital practice. This surface is the palm of the hand. The palm of the hand is different from other skin sufaces in that the epidermis is thick and makes it of little use in the regulation of body temperature. For this reason, vaso-dilation and constriction under the influence of heat and exercise is less useful physiological and does not occur to the same extent as it does in other skin areas. The fact is, that under normal conditions in normal individuals, the color of the palm of the hand varies remarkably little at different times of day and from day to day. I have compared my own palm with that of several normal assistants a great number of times and find them always almost exactly the same.

To estimate color in a patient, the physician must first be sure that his own color is normal. One can gain an idea concerning this point by comparing his own palm with those of a number of young healthy individuals. If the physician's palm is found to be normal in color, it can be used for comparison with patients: To make the tests, both physician and patient must sit or stand comfortably, each having his hand at about the level of the apex of his own heart or possibly an inch lower. The hands should be semi-flexed and allowed to remain in this position for a few moments until constant color is established. The comparison may then be made. A slight grade of anemia or plethora is so apparent on comparison that it could not escape the notice of even a most casual observer. The removal of as little as two or three hundred cc. of blood by venous section or the addition of two or three hundred cc. of blood by transfusion gives rise to a change in color which could not escape the notice of a casual observer.

I can assure the reader that this method is dependable if made carefully and if the physician has had a little experience. It is well worth

while for any physician to get acquainted with the method and use it with confidence. In my hands, it is equally as valuable as the determination of a red count or percent of hemoglobin if not more so, and is at the disposal of every physician whose own color is normal. It requires no appâratus and only a moment's time. This method has been described in more detail in a previous paper (2).

Given the fact that because of abnormal pallor of the palm, we make a diagnosis of anemia, we should next concern ourselves about the type of anemia which afflicts the patient, for upon the type depends our choice of methods of treatment. This can be determined in a majority of cases through estimation of the blood counts and by examination of a stained blood smear. In the secondary anemias, we have a relatively greater reduction in the hemoglobin percent than in the red count associated usually with a polymorphonuclear leucocytes. In aplastic anemia, we have a reduction in all the formed elements of the blood, red cells, white cells, and platelets. The same status of affairs may be observed in pernicious anemia except for the fact that the reduction in white cells and platelets is not inclined to be so great and the red cells show a distortion in shape and size which is very characteristic of the disease. Most important in this illness is the increase in diameter, thickness and opacity of the red cells. This (so-called makrocytosis) can be observed in the early stages of the disease and is so characteristic as to make it possible to diagnose the disease from a blood smear long before the red count is materially reduced. In fact, I have observed it frequently as long as six to eight years before the patient became definitely anemic, in fact once when the patient was polycythemic to the extent of a red count of six million five hundred thousand. The finding coupled with an achylia, a history of tingling in both hands and sore mouth should enable one to predict anemia positively one or several years before it appears.

The leukemias can be diagnosed by the finding of a distortion of the differential white count or in the appearance of pathologic white cells. These facts are so familiar to internists that I need only mention them in passing.

There is one type of anemia which I should like to more than mention. This type is pernicious anemia. I could say nothing in this paper which would interest internists in the diagnosis of pernicious anemia after the anemic stage of the disease has been reached. It seems a crime, however, to allow the diagnosis of pernicious anemia to be delayed to any such advanced stage as this. Discovering a case of pernicious anemia after the patient has become anemic is exactly analogous to discover a case of tuberculosis after it has progressed to such an extreme advanced stage that the patient has huge cavities, high fever, emaciation, and is about ready to pass out. Tuberculosis should be diagnosed in its early stages if one wishes to obtain a maximum result so far as the prolongation of a useful degree of health is concerned. Exactly the same statement can be applied to the diagnosis of pernicious

anemia. It should be diagnosed eight or ten years prior to the time at which the patient becomes anemic, and at such a time it is relatively easy to make the diagnosis practically with positiveness. I wish to emphasize the fact that the diagnosis can be made at this early stage with such accuracy that the patient can be told almost positively he has a potential anemic case and that he must constantly concern himself over matters which may percipitate the condition, matters such as restrictions in diet, infections, mental or physical strain, and excessive exposure of the skin to sunlight.

In almost every patient who has pernicious anemia in the anemic stage, one can get a long history of symptoms which are characteristic of the disease which date back five, ten or even twenty years and make one realize that the average case of pernicious anemia should be diagnosed positively at the time of onset of these symptoms and not at the time of onset of the anemia. In the average case which is diagnosed on the basis of blood findings, we find a history of symptoms such as tingling of the finger tips of both hands, sore mouth, dyspepsia, characteristic of achylia, and diarrhoea characteristic of achylia. In patients who come to a physician complaining of dyspepsia, diarrhoea, peculiar feelings of nervousness or weakness, or sore mouth, one should always inquire concerning numbness and tingling in the finger tips and toes. There are very few common illnesses except pernicious anemia which give rise to numbness or tingling in the finger tips in both hands and especially in finger tips and toes on both sides. This phenomenon is most characteristic of impending pernicious anemia especially if it is inclined to be persistent over several weeks or months. Furthermore, aphthous stomatitis and a beefy red appearance of the tongue is most characteristic of this disease. In fact, a red tongue especially if furrowed and dry and especially if associated with atrophy of the papillae is as characteristic of impending pernicious anemia as a markedly reduced sugar tolerance is characteristic of diabetes. Dyspepsia associated with a total lack of hydrochloric acid in the stomach juice is found in almost every case of pernicious anemia after they have become anemic. It has been found in almost every case of pre-anemic pernicious anemia (diagnosis proven by later developments) which I have observed. A few have shown marked subacidity with a later development of achylia. Makrocytosis previously referred to occurs in the earliest stages of the disease. There is, furthermore, an increased opacity and blueness which characterizes the appearance of the red cells which can be observed with great definiteness and which to me indicates that the average red cell is closer than usual to the normoblast. The increased opacity and blueness which characterizes the makrocyte as compared with a normal red cell characterizes also the blasts as compared with normal red cells.

The above syndrome of symptoms can often be observed in the family of patients who have advanced symptoms of pernicious anemia. The symptoms, furthermore, tend to vanish on

a Minot-Murphy Diet. For early cases, this usually takes a period of about two months or more. The only cases of aphthous stomatitis which I have actually benefited by therapy have been cases of this sort which I have found to be associated with achylia and other symptoms which I thought indicated that that patient was a potential case of pernicious anemia. In these, the stomatitis has been relieved by liver.

Symptoms which occur at a later period but which âlso antedate the onset of the anemia for one or several years, are atrophy of the papillae of the tongue, disappearance of the normal roughness of the skin of the forehead, a tendency to a ruby-like transparency of the lips (caused no doubt by atrophy of the epithelium of the lips), and a tendency to vague pains between the joints which cannot be accounted for by arthritis, subdeltoid bursitis, or other anomalies of the sort. It is by no means uncommon for a patient in the pre-anemic stages of pernicious anemia antedating one or many years the onset of the anemia to complain of vague pains which may baffle the physician completely. The pain may be mild or in many cases may be very intense—in fact, in one patient observed by the writer pains in the extremities had been so intense as to confine the patient to bed for months at a time. The case had been diagnosed multiple neuritis by almost every physician who had seen her. In fact, this diagnosis was correct except in the fact that the primary source of the multiple neuritis had not been discovered until the patient was a total wreck—far beyond the desirability of prolongation of life. Even at this stage, the blood count was not materially reduced nor was the patient pale. Makrocytosis, achylia, stomatitis and atrophy, however, made a positive diagnosis as simple as abc.

As previously mentioned, in pernicious anemia there is a tendency for the large makrocytes to lodge in the capillaries. This phenomenon gives rise to an abnormally red appearance of the patient and may for years obscure the real disease from which the patient suffers. This is abnormally marked if the superficial epithelium is atrophied to such an extent that the skin becomes translucent and allows the accumulated red cells to show their color more clearly. The average patient with pernicious anemia prior to the appearance of anemia or even after the red count has been reduced to three and one-half or four million or less has an abnormally red or ruby color. This may be unusually marked if the count is not reduced, or especially if it is increased, as it occasionally is, to five ând one-half million or six or even six and one-half million. In cases of this sort, one can convince himself of the existence of an impending anemia by comparing capillary blood with venous blood. The diagnosis of the condition in this stage is most important because of the fact that it is in this stage that most can be accomplished so far as the prolongation of a useful state of health is concerned. There is generally and unfortunately a mental deterioration which accompanies pernicious anemia and which may appear at an early stage. It gives the

patient a child-like personality and manner of speech which to me indicates deterioration of cortical cells and which if once thoroughly and well established is likely to persist. If we are to prevent the development of mental changes and cord changes which cannot be cured by transfusion, liver therapy, or what not, we must discover the disease before an advanced stage is reached, that is before these changes have manifested themselves as an evidence of actual cell deterioration.

The fact is that the disease can be discovered easily and with definiteness in the pre-anemic stage and I firmly believe that it is as urgent for the physician to discover cases in their incipiency and to get them under a useful method of therapy, âs it is to discover tuberculosis in its incipiency and to get the patient under proper treatment before irreaparable damage has been done.

This paper has been largely devoted to the diagnosis of anemia for as previously mentioned the treatment of anemia has been dealt with at length in recent literature. I feel that liver therapy has a most important place in the treatment of anemia especially in the pre-anemic stages. I feel sure also that it has a permanent place in the treatment of pernicious anemia after the anemic stage has been reached. I do not feel convinced, however, that transfusion should not also be used and pushed to the point of restoring a reasonably normal color in the paler patients. It hastens recovery and does no harm, if the size of the transfusion is kept below a point which causes capillary hemorrhage. Massive transfusions in pernicious anemia are dangerous. Transfusion of one or one and one-half pints at three or four day intervals repeated to the point of nearly restoring, but not completely restoring normal color in the palm of the hand is a safer procedure especially in the more severely ill patients. No effort should be made to restore the red count by this means, for so long as a patient has makrocytosis he is better off with a red count of three or three and one-half million than he is with a count of five million. This statement is based upon a very broad clinical experience in which transfusions were used consistently for many years before the advent of liver therapy. In the presence of marked makrocytosis a count of five million to me indicates plethora and an unhealthy situation. I have known of advanced cases with extreme makrocytosis in which color was normal and the patient better off when the count was as low as two million five hundred thousand.

Whereas, some physicians have questioned the usefulness of transfusion in the treatment of pernicious anemia, none could with reason question the usefulness for transfusion in the secondary anemias and aplastic anemia and in severe anemia caused by leukemia. In the secondary anemia, transfusion is an immediate and permanent cure if the cause of the anemia can be found and removed. It is a complete cure if pushed to the point of restoring normal palm color. It is absolutely safe if the donors are properly typed and can be pushed to large volumes without harm. This

represents one of the most sensationally specific, quick and complete cures with which we are acquainted in the practice of medicine. Out of a great number of cases which I have transfused, I do not know of one solitary case which has been harmed by it and nor do I know of one solitary case which was not permanently or temporarily benefited by the procedure.

The indications for transfusion are two-fold if the patient has â debilitating disease such as typhoid, tuberculosis, chronic bleeding ulcer, or a debilitating disease. Here it is urgent that the tissues be supplied with a quantity of normal corpuscles adequate for the purposes of supporting a normal functional capacity of the organs and for the healing of tissues.

Conclusions

Anemia can be diagnosed simply and accurately by examination of the color of the palm of the hand according to a technique which is described.

Pernicious anemia can be diagnosed with definiteness many years before the anemic stage is reached—in fact pernicious anemia is a very chronic disease, the anemic stage of which could almost be called a terminal event. Treatment in the pre-anemic stage is most satisfactory and prevents the development of brain and cord lesions and other complications which when once established do not yield well to therapy of any sort.

Transfusion hastens recovery of advanced cases, but must be used with care in pernicious cases. My results agree with those of other observers concerning the usefulness of liver therapy.

Transfusion is an immediate, complete, and safe cure for secondary cases and chlorosis and is permanent if the primary cause of the anemia can be found and removed. It is the prince of all specifics if strongly indicated and if technique is flawless. It is especially indicated in debilitated cases and in patients who have other diseases which demand an adequate supply of blood to the tissues for prompt function and prompt healing.

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Liver Diet in Pernicious Anemia*

By Hilding Berglund, M.D., *Minneapolis, Minnesota*

I WILL confine myself to a few points I wish to bring out. Yesterday you had the opportunity to listen to the splendid presentation of Dr. Sturgis, relating in a clear way the surprising and satisfactory results that one, as an unbroken rule, meets when treating pernicious anemia with raw calf liver, or with the liver extract that is now available, thanks to the work of Dr. Kahn operating with Minot and Murphy. I will only add that there seems to be some differences in the results obtained. We had better be careful in our statements because we have such short experience so far that those of today may be amplified by further experience. There is some difference between the treatment with raw liver and that with liver extract; this is not surprising when we consider that the liver in the body is an organ which contains the greatest number of powerful enzymes. The difference seems to me that when we feed raw liver when the patient is about halfway back to normal, there seems to be, without any exception, the development of marked eosinophilia, which may reach 4,000 cells per cm. This we have not met in any case treated with liver extract.

We also have to remember that the liver extract we are using today is not at all a definite product. The purification is going on in Dr. Kahn's laboratory, and instead of the yellow powder, Dr. Kahn has now produced a white amorphous powder with less than one-half gram per cc., with correspondingly less active power.

What do the wonderful results we obtain mean when we try to correlate them with our results in pernicious anemia? It is important to remember that what we call pernicious anemia is a disease characterized by much more than the anemia. The three important features are the achylia, the subacute combined degeneration of the spinal cord with changes in the central and peripheral nervous systems, and the anemia. The question immediately presents itself, which of these symptoms is influenced by the liver diet? Then it seems clear that only the anemic condition is influenced. The achylia remains unchanged after the patient's blood has entirely recovered. Many of you have already seen that in the cases that show the beautiful improvement of the blood the spinal cord symptoms may continue to progress, sometimes rapidly. Also, that we get a

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response in the blood in cases in which there is not only very little change in the blood picture, but also with the most outspoken nervous symptoms. The patients are invalids, and yet the blood picks up in an entirely independent way. This is not without importance in our attempts to define the nature of the whole picture of pernicious anemia.

How long will this improvement last? Evidently no one knows, since the liver diet has been used only three or four years and the extract less than a year, but so far we know of no reason why it should not be continuous with the continued administration of liver extract even after the blood has returned to normal. It should be possible by the continued administration of extract to keep the blood permanently in a satisfactory or normal condition. The experience of the next few years will prove whether this position is correct or wrong.

What other anemias are influenced by the liver extract? As far as we can to date express an opinion the only anemia that is influenced is the anemia that we know in the last few years as more or less identical with the blood picture in pernicious anemia.

As to the secondary anemias, what of those? There we have to consider that what we call secondary anemia is far from a uniform group. They undoubtedly contain many different things, but so far as the blood formation and the blood picture goes they should fall into one group. I have had, and others have had a not too limited experience with the secondary anemias that one sees in middle aged or a little less than middle aged women. I have studied such patients and in my experience the patients have been more or less coöperative. I have tried the raw liver and we are now trying the liver extract, but in spite of adherence to the liver diet for weeks or months it has left the anemia untouched. There are a few cases that might be thought to respond, but there are cases that by competent hematologists one year are diagnosed as secondary anemia, and the next year as pernicious anemia. These cases are rare but they have been observed by hematologists in different parts of the world.

Where does this lead us in regard to a theory for the action of the liver extract? Minot and Murphy have suggested that the chief action is the bringing about of the final stage of maturity of the red cells. This is attractive if we consider that the bone marrow is filled with bright red cells crowded with hemoglobin, but also containing a nucleus which the bone marrow is able to finish and get rid of the nucleus and discharge into the circulation. If we consider that what is being done by the liver is the maturing of the cells, that is an attack on the finishing of the red cells, we should think that the extract contains a normal body constituent that perhaps has nothing to do with pernicious anemia. If that is true we should expect to obtain similar results with normal individuals. In our laboratory three of our staff, two ladies and one young doctor, all healthy individuals, have been taking three vials a day of the liver extract.

We have not had so much response of the reticulocytes as in pernicious anemia, but there has been a rapid increase in the red cells, from 4,200,000 and 4,500,000 before the diet, up to 6,200,000 and 6,600,000 on the tenth day. Then, in all of them it dropped to the neighborhood of 5,000,000 on the seventh day, and then up to 7,000,000. We are continuing these experiments on normal individuals, but it has been difficult to obtain the liver extract in sufficient amounts.

This little observation is, I think, of great significance because it confirms our previous assumption that the liver extract is something that normally plays a rôle in the final maturing of the red cells.

Can we go any further in our theory? I think we can, even if it takes us into still deeper water. When the body develops there is, of course, a morphological development and a chemical development. Ordinarily when we study our body we see the morphological and the chemical developments going parallel in a normal way. During the blood formation in the fetus when the primitive blood formation takes place the chemical development is ahead of the morphological development; so that the cells are crowded with hemoglobin in their development, when the nucleus is very immature. Therefore, in the embryonic life the chemical development of the blood is ahead of the morphological, but later on we get the normal blood picture. In pernicious anemia, as Ehrlich brought out in the '80's, we revert to the former condition, so that the hemoglobin then seems to be undisturbed. Every cell contains enormous amounts of hemoglobin that make the cell larger. In pernicious anemia we seem to be able to interpret that as a return to the morphological element of the cell rather than the chemical element. In the secondary anemias we have the contrary. There is no disturbance of the primary character in the morphological red cells, but a definite weakness in the manufacture of hemoglobin. That is why we call it a secondary anemia with low index.

If this outline is correct, then we should not expect to get any effect of the liver extract on the chemical manufacturing process. It therefore should leave the secondary anemia untouched, since it evidently affects the morphological phase of the blood formation in pernicious anemia. It is the morphological phase in which we have our trouble.

You will make the criticism of this suggestion that it is made after we have made our observations. Evidently it is, as with most theories. It is also clear that it is vague and the only excuse for taking your time to listen to it is that it may serve to stimulate thought. The fact that we have come up against such interesting facts as we have in the liver diet should not be held against the speaker. It proves in the best way the magnitude of the discovery of Minot, Murphy and Kahn.

The Scientific Spirit*

By Professor Marten ten Hoor, *Tulane University, New Orleans, Louisiana*

WHEN a layman enters the professional presence of a physician, he does so in humility, and possibly even in fear and trembling. Since even a philosopher or a student of philosophy cannot endure the toothache or any other ache patiently, he must also occasionally enter this imposing presence and he too cannot but experience this feeling of timidity, a timidity not unlike that of the penitent approaching the confessional, since it has for its cause fear of the coming diagnosis and of the subsequent prescription of treatment. When a student of philosophy has the temerity to address a whole "College" of physicians, his fears are not only quantitatively multiplied but they are also qualitatively altered, because to his natural layman's respect for the professional expertness of his audience there is added, as a complication, considerable doubt as to the attitude of his audience to philosophy.

Philosophy has a rather mixed reputation with the layman. Those who have never studied the subject either have a tremendous respect for it or they have no respect for it at all. Those who have studied it systematically and intelligently have their respect tempered with a certain amount of decent disrespect. Some of these serious students of philosophy are even inclined to agree with Omar when he says,

"Myself when young did eagerly frequent
Doctor and Saint, and heard great argument
About it and about; but evermore
Came out by the same door wherein I went."

There are even apostates who have come to accept Michelet's dictum that "metaphysics is the art of systematically deceiving oneself."

However, the timidity which I as a layman and as a student of philosophy feel in your collective professional presence is as nothing compared with the fear and trembling which, as a boy, I used to experience in the presence of a quite different kind of internist. In my boyhood our family was visited, once a year, by the minister, on the occasion of what was known as "house-visitation." At this time all the members of the family were subjected to a searching spiritual examination, to be followed by diagnoses of the states of our respective souls. Finally, treatment was

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prescribed where necessary. I assure you that our childish fear of the mysterious knowledge and desperate technique of our family "physician of the body" was as nothing compared with our fear of the powers of this family "physician of the soul."

Now in our day no one would ever think of confusing these two types of "physicians," so sharply have their respective techniques and their professional activities become differentiated. In fact, sometimes their contemporary relations are not entirely amicable. And yet they were at one time one and the same individual. I propose to introduce my topic with a brief and somewhat playful survey of the history of the changing relations of these two types of "internists."

In the person of the primitive "medicine man" we find the ancestor of both types. This versatile dignitary attended to the needs of both body and soul, his technique being a combination of magic, incantation, and native shrewdness. But soon there occurred a phenomenon analogous to cell-division and differentiation of function so characteristic in the development of organisms. The medicine man "divided" into two: the ancestor of the physician of the body as we know him, and the ancestor of the physician of the soul. The latter soon developed into a philosopher-theologian who seems to have been the spiritual progenitor of the house-visitor of my boyhood. Each of these two new professions claimed diagnostic and therapeutic powers.

This division of interest and of labor was sharply emphasized by mediaeval theology, with a consequent evaluation and ranking of the professions quite different from that generally accepted in our day. The body was adjudged of the earth earthy and, since it had only a short while to live, of temporary importance only. Affliction and disease were accepted with equanimity; by some enthusiasts even with rejoicing, since it was believed that God thus punished those whom he loved. Philosophy, which was in this period the humble handmaiden of religion, sought, and thought it had found, theoretical justification for this discriminative attitude to the body and to the profession attending its ills and ailments.

The physician of the body was naturally at a tremendous disadvantage. What, after all, was a temporary bodily pain—or even a lifetime of bodily suffering—compared with eternal damnation? When considered professionally, the physician of the soul had a great advantage. In diagnosis, all symptoms indicated one and the same ailment: original sin. The physician of the body, on the other hand, was faced daily with a baffling number of diseases; in fact, new ones were constantly appearing.

In the matter of treatment, too, the physician of the soul had a great professional advantage. The treatment for original sin was the prescribed way to salvation. There was ready an accepted body of revealed doctrine to guide the profession. No new treatments were permitted. Originality in this meant excommunication at least. Every bishop was a kind of sanctified Dr. Fishbein. The physician of the body, on the other hand,

had no choice but to work out his problem empirically. There was no official materia medica, not even much of an unofficial one.

In professional standing the physician of the soul stood supreme, since he had a divine commission, received and insured through the mediation of the church hierarchy. The physician of the body sometimes did not even have a diploma. In the matter of results, it was again the physician of the soul who had the advantage. Strictly speaking, he never lost a patient since the soul was immortal. Consequently he took no risk in prescribing and he never had to attend post-mortems. Nor could the patient's permanent condition after treatment be ascertained since sooner or later he left for another world. The physician of the body, on the other hand, lost an occasional patient, to put it mildly. His failures were recorded in marble and stone. Even his successes were insecure, since relapses were possible.

The result of all this was that there was little official encouragment, by religion and philosophy, of scientific observation and experiment in medicine. Philosophy had little interest in science. But then came the next stage: Philosophy declared its independence of theology because it resented the constraints put upon it and insisted on trying its own wings. One of its first attempts at independent investigation was directed at the analysis of the soul. Thus psychology developed.

But then a very interesting thing happened. The soul, which was the patient being diagnosed, did not exactly expire during diagnosis, but what was much more embarrassing, it evaporated. Psychology tried to be scientific and independent and promptly lost its bearings. Ever since this embarrassing disappearance of the patient, psychology has had a rather exciting and disturbed career. Having found the soul too volatile or too ethereal for scientific study, it announced that it was engaged in an analysis of mind. But this concept, too, it found embarrassing and difficult of definition, and so substituted for the concept of mind the concept of consciousness. In our day even this has been discarded, the psychologists—at least some of them—insisting that psychology is nothing more than the science of behavior. A wit has epitomized this history of psychology thus: "Psychology first lost its soul, then it lost its mind, then it lost consciousness and now it has only behavior left."

Fortunately, this experience with the attempt at a purely theoretical analysis of the soul taught philosophy a lesson: the need of a new intellectual spirit and of a new method. While philosophy had been learning this lesson, science had been quietly and steadily developing as an object lesson in the new spirit and the new method, thus adding a moral to the tale. Whereupon there arose among philosophers an enthusiastic—in fact, possibly a bit over-confident—exponent and champion of the scientific spirit and the scientific method, Francis Bacon. Since Bacon's day, philosophy has never entirely resigned this rôle and in our own day there is probably no problem in which philoso-

phers take such enthusiastic interest as the problem of science.

This history is to us moderns only mildly interesting, so accustomed have we become to the acceptance of science and its methods. The old quarrel between science and religion seems out of date, even when it is revived and when it becomes for months the featured news in our public press. Yet we must not forget that the quarrel had its tragic side. Many obstacles were placed in the way of free scientific development. Scientists were ruthlessly suppressed and even persecuted for their loyalty to their ideals. But the victory of the scientific spirit cannot be denied. Such a meeting as this is eloquent testimony to this victory, and hence it seemed to me a fitting occasion for attempting a brief analysis of this spirit.

What is the scientific spirit? Let us examine it by contrasting it with the spirit which so long opposed it, which we may call, for purposes of identification, the dogmatic spirit. From one point of view, both seem to be mental tendencies or attitudes; from another point of view, they seem to be mental habits. The dogmatic spirit begins with certain principles which are accepted as true on some other ground than observed or experimentally demonstrable and verifiable facts. Hence we call such principles, "dogmas." The facts are subsequently interpreted in the light of and in terms of these dogmas. The following illustrations exhibit the dogmatic spirit: (1) The scientific theory that some diseases are the result of the more or less accidental introduction of micro-organisms into the body was at one time emphatically opposed by certain theologians, on the ground that disease was a special punishment sent by God and that therefore it could not be the result of accidental infection. Granting for purposes of economy in this discussion that the dogma and the theory are contradictory, we cannot fail to note the surprising indifference to scientific observation and experiment here exemplified. (2) As late as the early 18th. century the following argument was advanced in defense of the Principle of the Conservation of Energy, a principle which was later experimentally demonstrated: "There are two ultimate principles or elements of Being, Matter and Energy. Now we already know that Matter is conserved. If God created Matter so that it could not be destroyed, how much more certain must it be that Energy, which is the spiritual principle, cannot be destroyed." (3) The third illustrâtion is contemporary and is advanced, incidentally, to exhibit the extravagances being perpetrated by enthusiasts in the field of psycho-analysis, as well as primarily to give an example of the dogmatic spirit at work. If you should go to one of these enthusiasts and report that you had had a dream featuring a bearded cow eating pink apples under a huge tree on a beautifully rounded hill, it would certainly be interpreted to mean . . . well, let the reader give his own interpretation, being sure thât the heart of it is a sex-complex, the more scandalous the better. It seems to me that we have here a good illustration of the habit of beginning with a dogma and interpreting facts in terms of it.

The scientific spirit or habit of mind, on the other hand, begins with brute facts, whenever possible; then proceeds to tentative principles, which are called hypotheses, and then returns again to facts. Now at this point I might well be interrupted with the question, "But what is a fact?" In a meeting of philosophers I would scarcely have dared to use such a simple term. If I did inadvertently do so, it would mean, as far as the real subject of the discussion is concerned, a profitless evening and a sleepless night. However, I have no professional scruples here and I don't mind indicating in a very simple way what I mean: If you drink some carbolic acid and subsequently suffer agonizing pains, I take the acid before you to be a fact, also the drinking of it, also the pain and the connection between the two. If you see evidences of much philosophical looseness here and are still in doubt, you have the first symptoms of the disease known as philosophy.

The scientific spirit or habit of mind we may profitably analyze a little further. The following characteristics can be analyzed out: First of all, the scientific spirit is *interested in facts*. Strange as it may seem to the neutral observer, there are minds which are not interested in facts; they are interested rather in protecting their own dogmas. To facts, when they seem dangerous, they take the defensive attitude, which makes their minds impervious to just those facts which they ought most to notice. There are even people whose immunity to facts is so complete as to be almost pathological; facts do not count in their thought and in their conversation, and sometimes not even in their practices.

Secondly, the scientific spirit is *interested in all facts*. Some people seem to have a blind side to facts, an affliction which is very handy and which often contributes much to the "spiritual" satisfaction and comfort of such individuals. The fact that minds do have such blind sides may help to account for the fact that statistics are so much more useful to the intemperate reformer than to the scientist.

In the third place, the scientific spirit *observes* facts. It trusts the senses because it is convinced that they are our only refuge where facts are concerned. However, it knows the limitations of sense-perception and is aware of the errors and fallacies which threaten the mind, but it seeks constantly to reduce this margin of error. It consciously and willingly gives up absolutism and is able to live at peace with relativism. It is not even afraid to confess a certain sane and courageous skepticism, confessing with Goethe that "man is not born to solve the mystery of existence, but he must nevertheless attempt it, in order that he may keep within the limits of the knowable."

The scientific spirit, in the fourth plâce, is interested in the *analysis* of facts; that is, it is interested in reducing facts, wherever possible, to simpler and more fundamental facts. The discovery of the disease we now call typhoid fever was no doubt important; but more important was the discovery of the bacilli which we now know to be the cause of the disease. Man's understanding and control over nature increases with analysis, and this manifes-

tation of the scientific spirit brings us close to the heart of science.

Fifthly, the scientific spirit seeks to *relate facts to one another,* the particular type of relationship which science is most interested in establishing being that of cause and effect. Charles Darwin insisted that a good scientist must be a good theorizer as well as a good observer. He not only here emphasizes the need of relating facts to one another but he also implies that the first attempt at establishing such relationships is always an hypothesis. It is to the point here to recall that such hypotheses and theories are not dogmas, the difference between dogmas and scientific theories being that the former are at once accepted as true and are not derived progressively from facts whereas the latter are so derived and are not at once accepted as true.

Hence the sixth characteristic of the scientific spirit: the scientist insists on *checking his theories against the facts.* Obviously, this task is never finished, since all facts are never at hand. New facts are constantly being discovered and thus the adjustment and readjustment of theories is made necessary. Finally, the scientific spirit is willing to *submit* to facts. This lesson science has learned only after long, and sometimes bitter, experience. It is hardly necessary to point out that in many fields of human inquiry and human endeavor this lesson has not yet been well learned.

When presented in this rather sophomoric way, the scientific spirit seems very reasonable and the dogmatic spirit very unreasonable. But we must not forget that *we* have several centuries of the development of science and the scientific spirit behind us. Nor must we forget, in this connection, that the dogmatic spirit is an insidious habit of mind which, in spite of its unreasonableness, has greatly influenced human thinking. The virus of dogmatism was in some way introduced into philosophy, literature, religion, and even science, and the disease, if we may for the moment call it so, held full sway until the scientific spirit was developed as an antidote. It is with the scientific spirit that the dogmatic spirit must be combated, wherever and whenever men are interested in the discovery of truth. We may be sure that there will always be occasion for combat, since the dogmatic spirit is the expression of the tendency, or possibly *is* the tendency, to defend our religious, moral, social, artistic, and political prejudices.

But the scientific spirit also has its dangers. There is the tendency to forget that inference from facts is always tentative. Science has often brought trouble on itself by assuming an attitude very much like that of the dogmatic spirit. The scientist must never forget that science is cumulative and progressive, and that scientific knowledge is relative and not absolute. Therefore science must always be in a receptive and welcoming mood towards new facts or new analyses of old facts. Science is largely a history of readjustments, corrections, and restatements, and there is no sound logical reason for assuming that this time is past or will ever be past. The history of medicine is as eloquent an illustration of this as it is possible to find.

The scientist must be quite as willing to give up old theories for better ones, old practices for new ones, the criterion

always being observation and experiment. "Back to Facts" must be the watchword of all science, possibly nowhere more than in the science of medicine. Science must be kept plastic in the presence of the existing subject-matter, someone has said. Nowhere is blind orthodoxy more out of place or more dangerous than in the theory and practice of medicine. It must be remembered that heterodoxy is not always wrong. Many men now recognized as great scientists have been outstanding, almost "professional", heretics. Heresy hunting with all its irrationality and extravagances, with its native dangers and its unfortunate by-products, is always a temptation to any organized profession. The good fortune of medical science is that the persistence, the vitality, and the nearness of the facts will always act—and that rather promptly—as a check. But this assumes the interest in and the receptivity to facts named above as characteristics of the scientific spirit.

However, far be it from me on such an occasion as this to dwell at length on the dangers which beset the scientific spirit, either in medicine or elsewhere. It was my purpose rather to celebrate the success of this spirit and to express admiration for this spirit especially as it is exemplified in the science of medicine. Of course, as a student of philosophy it is gratifying to me to recall the part philosophy has played in the emancipation and consequent development of this spirit, and I hope you will forgive me if I recall to your mind such names as Francis Bacon, Huxley, Spencer, J. S. Mill, to mention a few of the Englishmen alone, and to remind you of the efforts they put forth to explain and defend this spirit and thus to help bring about the victory which we now assume as a matter of course.

Where the ordinary layman admires medicine only because it rids him of his aches and pains, the "philosophical" layman, in addition, *and as a philosopher or a student of philosophy,* admires medicine because of the scientific spirit by which it is inspired and directed. And this spirit has been most eloquently expressed in your meetings here. I know that laymen such as myself have found them a great source of inspiration, not only because of the painstaking research, the splendid results, and the faithful devotion to a task reported here, all of which are eloquent testimony to the scientific spirit of medicine, but also because of the fine fellowship of science expressed in your interest in one another's work, a fellowship most eloquently expressed in the splendid demonstrations of appreciation with which you have received the work of your distinguished guests and your distinguished members.

This good fellowship is such as to move a student of human affairs and human progress to regret that it is absent, in word or deed or in both, in so many other branches of human endeavor. We do not have it to this extent in philosophy unless all confess the same metaphysics; it is notoriously absent in politics; and the history of religion is sufficient evidence of its absence in this field. There is no record of a war fought between exponents of rival scientific theories. Opponents of science like to point out the fact that science has been used in war for pur-

poses of destruction. These critics should be reminded of the fact that on such occasions science has been employed in the name of ends supposedly nobler than the ends of science itself. It is such uses of science which strain the international fellowship of science, though only temporarily, after which the brotherhood returns at once to the common interest and the common purpose. This fellowship of science is a true expression of the common interests of man; we may even say, of the brotherhood of man, a phrase which we use so much but put so rarely into practice. It is a fellowship which is a happy by-product of devotion to the cause of science and to the scientific spirit and which might well take as its motto the words of Plato:

"THE DISCOVERY OF THINGS AS THEY TRULY ARE IS A COMMON GOOD TO ALL MANKIND."

Editorial

MEDICAL OBSERVATIONS IN HAWAII

II. *The Early Manifestations of Leprosy*

The interest of the medical visitor to Honolulu turns naturally to leprosy, first of all, as the most advertised disease to be seen in the Islands. The tale of the leper is so bound up with the history and romance of Hawaii, from the time of the early missionaries and Father Damien down to the stories of Jack London, who certainly had a more accurate knowledge of the clinical aspects of leprosy than we might expect from a writer of fiction. To the average educated citizen of the United States the word Hawaii invariably suggests volcano, pine-apple, sugar cane, ukelele, surf-riding and leprosy. If we added anything more to this list it would probably be, interestingly enough, hula dancing and missionaries. The inevitable association of leprosy with Hawaii has an ironic tragic aspect; leprosy was not indigenous to the Islands, but, it is believed, was imported from China. In the Polynesian native race it apparently found a favoring soil, so that today, in spite of the large numbers of Chinese inhabitants, it is the native Hawaiian, or his hybrids, that constitutes the major portion of the sufferers from this infection. In Michigan I had come into contact with about thirty cases of leprosy during the last twenty-five years, but with one exception these were all advanced cases, typical textbook pictures, of leonine facies, the one exception being a generalized tubercular type of the disease of several years duration. When one's acquaintance with leprosy is based upon the advanced form, he has, as I discovered in Honolulu, a very inaccurate and incomplete conception of this disease. Indeed, he cannot be said to know leprosy in its most active and virulent stage, the most important one as far as diagnosis is concerned. Through the most kind courtesy of Dr. J. T. Wayson of the U. S. Public Health Service, I was given the opportunity of seeing at the Leper Receiving Station in Honolulu a wonderful clinical demonstration of the earliest manifestation of leprosy. There were about one hundred and seventy cases in this hospital at the time. The great majority of these were Hawaiians and part Hawaiians, a small number were Orientals, and only a few were Caucasians, Scotch, German, Scandinavian and American. To the station are sent all new and suspected cases for a confirmation of diagnosis; for preliminary observation and treatment, to be latter transferred to the Leper Colony on Molokai, should this be considered necessary. From the cases

at hand Dr. Wayson selected individuals, or groups, showing the very earliest recognizable lesions in different stages of evolution and resolution, and the varying forms and degrees of pigmentation and depigmentation. This was a clinical demonstration of extraordinary interest and the pictures of the disease presented here were so new and striking, and so unexpected as cardinal features of its symptomatology, that it was like the discovery of a new disease entity. These early lesions of leprosy are not adequately presented in any textbook, to my knowledge; and some of the most striking ones are not mentioned anywhere in the literature of the disease. The clinical pictures drawn of leprosy in the current textbook articles are nearly all based upon the well-established and advanced stages of the affection, and give no hint of the wholly dissimilar lesions of the early stages. Yet it is in these early stages that the fight of the human organism against the progressive bacillary invasion is so strikingly shown. After one has seen a large collection of lepers and has studied them collectively, the old clinical classification of different forms of the disease, based largely upon the symptoms of pigmentations, anesthesia, nerve involvement, nodule-formation, etc., appear to be illogical and unnecessary, since all of these apparent varying forms are simply the result of degree of invasion, and are dependent almost wholly upon the progression of invasion and the individual susceptibility, rather than upon any special pathological character of the individual case. There is no hard and fast line of demarcation between any of these chief symptoms of leprosy. They may all occur together at the same time, or may follow one another; at some time in his career the leprous patient will have experienced all of the type-symptoms or phases of the disease. It is misleading, therefore, to depict separate clinical and pathological types of leprosy as having any distinct entity. The disease should be regarded from the much broader standpoint of a progressive generalized invasion varying in time and degree in various localizations. From the old textbooks one also gets the idea that the development of leprosy is an extremely slow affair, extending over many years, and, therefore, that it is not likely to develop in childhood or early adult life. There were a number of young children in the Receiving Station at the time of my visit, and, if I remember correctly, Dr. Wayson told me of a case of a leprous baby of eleven months of age. Moreover, the appearance of well-defined leprous lesions may be very sudden—a few months, a few weeks, even a few days, may be the history of individual cases. In one case seen by Dr. Wayson the lesions had appeared only four days previously. In other cases the history may be that of a first crop of lesions seen many years ago, their complete disappearance for years, and then a sudden reappearance. These long spontaneous remissions are very disturbing in their possible relation to any supposed therapeutic effects. In one case seen at the sta-

tion, supposedly a recent acute invasion, a history was obtained of the occurrence of skin involvement of urticarial nature thirteen years previously, which Dr. Wayson believes to have been the first clinical evidences of the infection in this patient. The early skin symptoms are of a surprising nature, and can easily be mistaken for a number of non-leprous conditions. One of the typical early lesions is the so-called "bee- or wasp-sting." It looks precisely like a bee-sting; a reddened, slightly swollen area with a central lighter point. They look also like mosquito bites or hives that have been slightly rubbed. Other lesions resemble ringworms so closely that errors in diagnosis may easily occur. All of the forms of mycotic dermatitis and pruritus show the same close clinical similarity. In the cases in which the first symptoms are quickly followed by a long period of remission the diagnosis of an acute exanthem, particularly measles, might be made. A differential diagnosis between early leprosy and syphilitic rashes may also be very difficult. The final proof is, of course, the bacillary demonstration, and no early case should be definitely decided as one of leprosy without the positive proof of the presence of acid-resisting bacilli in the skin lesions. The method employed at the Receiving Station is very much better than the usual biopsy excision of a section of skin which is fixed, imbedded and stained in sections for the bacilli. A small incision is made in the suspected cutaneous area with a sharp scalpel, the blade is slightly turned and withdrawn scraping the side of the incision. The tissue juice, cells and blood thus obtained on the knife blade are spread on a slide, fixed by heat and stained as for tubercle bacilli. If it is a case of leprosy the bacilli in such a smear are numerous and easily seen. The procedure is much less unpleasant for the patient than the excision, the slight cut heals rapidly, and the diagnosis can be obtained almost immediately. In the suspected cases sent to the Receiving Station over 98 per cent of these bacillary tests have been positive on the first trial. I was very much impressed with the allergic character of these early skin manifestations; they resemble local allergic reactions more than anything else, and, I believe, will be found to be such. It is interesting that if the incision test is made after the local lesion has reached its height of intensity which it may do in several days, the tissue juice obtained contains great numbers of "beaded" bacilli or disintegrating forms. The implication would be that some degree of local bactericidal immunity had been attained. During their evolution the early cutaneous lesions are not painful, but are tender when pressed upon, there is a sensation of tension and more or less pruritus. There is also more or less fever and general malaise during the invasion stage. As the hyperemia and edema disappear, pigmentation or depigmentation follows, and a certain amount of anesthesia, usually in the older portion of the area involved. The pigmentations and depigmentations vary greatly in character and degree,

and can in themselves be very confusing clinically. They may appear as macules, or in large patches. In themselves they cannot be taken as having positive diagnostic value, but in any suspicious case should be tested by incision and bacillary examination. One of the most interesting color phenomena of the invasion stage of leprosy is a peculiar bluish tone of the skin of the forehead. It is seen best by oblique light; it is a peculiar gray-blue metallic shimmer beneath the epidermis, it reminds one of the blue-line of the gums in lead-poisoning, but is more diffuse. It suggests a very finely punctate cyanosis. It is mentioned by Jack London in his tale of the Islands, "The Sheriff of Kona" as "the darkening of the skin above both eyebrows, just like the dimmest touch of sunburn—but that there was a shine to it, such an invisible shine, like a little highlight seen for a moment and gone the next." Another of the early clinical signs of leprosy is the peculiar blob-like enlargement of the ear lobe. It suggests the swellings of the skin in myxedema, and microscopically shows a proliferating granulomatous inflammation of the stroma of a myxedematous nature. Great numbers of bacilli are present in this stroma. This involvement of the ear lobe is also mentioned by Jack London in "Koolau the Leper" as a "bloated ear-lobe" flapping "like a fan upon his shoulders," and in "The Sheriff of Kona": "Yet there it was, on his brow, on his ears—the slight puff of the ear-lobes." The cord-like thickenings of the nerve-trunk so strongly emphasized by various writers as an early diagnostic sign of leprosy, were seen in the ulnar nerve of only a few of the cases examined. In one boy the enlargement of the nerve trunk was very marked. Marked neurotrophic changes were seen in the hands of two children, one a boy of 10-12 years showing a marked degree of this condition, so that it must be rated among the early symptoms. All of the symptoms described above occur as the first ones, before any deforming granulomatous development takes place. They constitute a clinical picture of leprosy quite different from that usually given by the textbooks. Unless one has actually seen these early lesions it would be extremely easy to err in diagnosis, and this is of very great importance because of a recent announcement that in certain portions of the South indigenous cases of leprosy are now being discovered. Advanced cases are always turning up in the hospitals of our large cities; while these usually conform to the classical textbook pictures and are easily recognized, it is a question of some significance as to how many early cases there may be in the country that have not been recognized. As to the results of treatment with Chaulmooga oil and its derivatives it would be premature to make any definite statement. That under such therapy marked remissions of the disease occur there is no doubt; the condition of the patient may be so improved than an apparent clinical arrest or cure is indicated, and the patient may be returned to his home on parole. In such patients

relapses may unfortunately occur. The situation is very much the same as in the case of syphilis and tuberculosis, an apparent clinical cure—the reduction of an aggressive infection to a latent stage—may be obtained therapeutically. This for leprosy is a great advance, not only as far as the patient himself is concerned, but as far as the protection of the community is involved. It will take a generation, or several, before the full worth of the present treatment of leprosy can be evaluated. Nevertheless, the reduction of so many active lesions to latent ones must have an effect upon the spread of the disease, and in regions in which the treatment is vigorously pushed over a long period of time the number of lepers should diminish rather than increase. As to any influence of a concurrent syphilis upon the lesions of leprosy, or of a subsequent leprosy upon the course of syphilis no definite information was obtained. Some observers believe that syphilis is often more malignant in a leper, leading to earlier ulceration and mutilation, and more rapid development of the leprous lesions. Other observers have not noticed any influence of either disease upon the other. Leprosy is a sinister infection. There is no recognizable local lesion of entrance of the infecting organism, as in the case of the primary chancre of syphilis. When the disease is recognized, no matter how early, it is already a generalized invasion. There is no therapy that will reduce the lesions of the disease quickly to a state of latency and clinical cure, as that of the arsenicals in the case of syphilis. The unpleasant clinical aspects of leprosy, its more certain recurrences after periods of latency and its more inevitable course make it to the popular mind a much more-to-be-dreaded disease than syphilis. When added to this is the growing certainty that the infection may at times be quickly acquired under certain conditions of exposure, and develop with a relatively rapid incubation the popular dread of the disease is more than justified. The Receiving Station at Honolulu offers a great opportunity for intensive research and study of this disease. With the present laboratory equipment and the lack of sufficient staff and funds this investigation cannot be carried out in an ideal manner, and it seems a great opportunity lost. If the Federal or local Territorial Government cannot finance such a research laboratory, surely here is a wonderful opportunity for some of the multimillionaire missionary families to take up again the good work of their ancestors and found such a laboratory for the Study of Leprosy. The memorial fund in the honor of Leonard Wood to be used in a campaign against leprosy in the Philippine Islands is a wonderful thing and should have its counterpart movement in Hawaii. The Receiving Station in Honolulu is doing fine work under its present handicap, for the daily practical demands upon the staff are so great that the purely scientific study must take second place. To Dr. Wayson and the other members of his staff I wish here to express my appreciation and thanks for their most kind and instructive demonstration of their wonderful material.

Abstracts

The Pre-operative Treatment of Graves' Disease by a Combination of Iodized Fatty Acid and Vitamins A and D. By GILBERT L. ADAMSON, M.D., AND A. T. CAMERON, S. Sc., F.R.S.C. (The Canadian Medical Association Journal, October, 1928, p. 420).

Harvey, in 1927, had noted that cod-liver oil (which contains some iodine) when fed to goats, causes passage of more iodine into their milk than when the equivalent amounts of potassium iodide and olive oil are fed, from which an effect of some specific constituents of cod-liver oil on general iodine metabolism may perhaps be adduced. It was suggested by Dr. I. M. Rabinovitch that Lugol's solution might be replaced by a preparation of iodized jecoleic acid incorporated with a vitamin concentrate from cod-liver oil—a preparation to which the trade-name of Vitiodum (Forte) has been given. Good results have been reported in cases of Graves' diseases to whom this preparation was administered instead of Lugol's, by Dr. Rabinovitch and Dr. Mason of Montreal. With the approval and coöperation of the Medical Research Committee of the University of Manitoba, Adamson and Cameron have carried out a series of tests that are now sufficiently lengthy to justify preliminary report. Their results showed that this combination of iodized fatty acid and vitamins A and D is at least equivalent in value to Lugol's solution in the pre-surgical treatment of cases of Graves' disease, though as yet little light has been thrown upon the mechanism of its action. This seems to suggest a new and desirable field of investigation into normal and pathological thyroid function. Vitiodum (Forte) is stated by its manufacturers (Ayerst, McKenna and Harrison) to consist of a gelatine capsule containing 275 units of vitamin A (U.S.P. technique of measurements) and not less than 75 units of vitamin D (as calculated by the non-official technique suggested by McCollum, Simmonds, Shipley and Park) together with iodized jecoleic acid in amount containing 0.03 available iodine, the equivalent of that present in 10 minims of Lugol's solution. These capsules dissolve in warm water liberating a greenish oil. No precipitate is given with silver nitrate, nor does the presence of acid liberate any iodine, so that the presence of iodide can be regarded as excluded. Analyzed by Kendall's precedure, figures for iodine content were found to vary from 0.02 to 0.03 grm., the lower figures being probably too low through the large amount of relatively volatile fat present. Jecoleic acid is an unsaturated acid of the type of oleic acid, with the formula $C_{19}H_{36}O_2$ in which the position of the double bond does not appear to have as yet been definitely ascertained, so that its formula can be written at present $CH_3(CH_2)_n$ Ch:CH.$(CH_2)_n$ COOH. Iodized jecoleic acid correspondingly is $CH_3(CH_2)_n$. CHI. CHI.$(CH_2)_n$. COOH. Because of the success of the pharmaceutical preparation in the first tests it was desirable to find out to which of the constituents the action was due. Accordingly tests were made on eleven patients using the vitamin fraction and the iodized fatty acid fraction. The tests in themselves are insufficient in number, but they suggest the strong probability that both the vitamin fraction and the iodized fatty acid fraction are necessary for definite effect. It remains to be determined whether both A and D or but one of them is necessary, and whether the iodized jecoleic acid can be satisfactorily replaced by iodides and other types of iodine compounds. From their series of cases the authors draw the following conclusions: Vitiodum, a combination of vitamins A and D and iodo-

fatty acid, is as effective as Lugol's solution when administered in Graves' disease, its beneficial action and the limits of its beneficial action closely resembling those of Lugol's solution. Vitiodum has not, in their experience, produced any gastro-intestinal disturbances during or following its administration. It is probable that neither the vitamins nor the iodo-fatty acid alone are effective. It is very desirable that further work be undertaken, not only to have records of a much larger number of cases accurately checked during vitiodum administration, but to investigate as widely as possible the relation between the vitamins concerned and thyroid and iodine metabolism.

On the Occurrence of Blood Dyscrasias Following the Administration of Neoarsphenamine. By W. ROLAND KENNEDY, B. Sc., M.D. (The Canadian Medical Association Journal, October, 1928, p. 439).

Within the last decade medical literature has contained from time to time reports of reactions with unusual blood pictures following the use of arsenical preparations in the treatment of syphilis. The first reports of such blood dyscrasias were made by Leredde and Labbe and Langlois in 1919. Kennedy reports the development in a patient in the course of antiluetic treatment with neoarsphenamine, of a hemorrhagic diathesis with bleeding from the gums, epistaxis and hematuria. There was no antecedent history of a similar character in either family or personal history. Of particular interest were the blood findings, a much reduced platelet count, a prolongation of the bleeding time and non-retractility of the clot. With cessation of bleeding there was a rapid return to normal of the blood platelets and bleeding time. In short, there existed a toxic thrombopenic purpura or purpura hemorrhagica. A review of the literature supports the view that neoarsphenamine and sulpharsphenamine are the culpable preparations and not arsphenamine. The blood dyscrasias developing in cases of syphilis under treatment with arsenical preparations fall into three fairly distinct subdivisions: Purpura, purpura with hemorrhages and aplastic anemia with hemorrhagic diathesis. The purpuric-anemic syndrome may follow either intramuscular or intravenous injections. That neoarsphenamine and sulpharsphenamine exert a toxic action of the bone marrow has been generally accepted. The blood picture and the bone marrow lesions are similar to those of benzol poisoning. These arsenical preparations in short exert a direct destructive action on leukocytes, platelets and red blood cells. The interference with the platelets causes the hemorrhagic diathesis, and the leukopenia and anemia result from the toxic action on the other elements, the white and red cells. In neoarsphenamine there is a double benzol ring, and the benzol radical is probably responsible for the pathological process, rather than any impurity in the drug, as has been assumed by some. The lesion, however, is rare. Prevention is the best remedy. The occurrence of mild nitritoid symptoms and slight purpuric lesions are a prodromal indication. Jaundice may also appear in like manner. In such cases arsphenamine and other antiluetic remedies can be safely used and should be substituted. As neoarsphenamine and sulpharsphenamine are arsenical preparations sodium thiosulphate intravenously is indicated, in increasing doses from 0.15 to 0.6 grm. in 20 per cent aqueous solution daily. In cases that develop a progressive anemia reported blood transfusions have been life-saving. These enable the patient to live while the toxin is being eliminated and the blood centers are thereby given a chance to regain their function. This process is usually slow except in young adults. It has been noted by Weil and Isoh-Wall that with transfusions convalescence is often obtained without relapse, but that in pernicious anemia transfusions are of no ultimate benefit.

The Epidemiology of Undulant (Malta) *Fever in Iowa.* By A. V. HARDY. (U. S. Public Health Reports, Sept. 21, 1928, 2459).

From July 1, 1927 to June 30, 1928 the diagnosis of undulant fever in Iowa had been established in 83 cases. 30 of these

cases were diagnosed during April, May and June, 1928. The cases occurred sporadically and were widely scattered. Multiple cases in one locality are probably largely explained by a greater accuracy in diagnosis. In two instances two cases occurred in one family. In another, a farmer and an employee who worked together but lived separately both acquired the infection. Forty-six of the patients lived on the farm, seven in towns of less than 1,000, and twelve in towns with a population between 1,000 and 5,000. Of the remaining 18 cases, seven lived in towns of over 50,000 population. Sixteen occupational groups were included. 39 were farmers, 6 farmers' wives, 1 farmer's daughter, 6 packing house employees, 10 housewives not living on a farm, 4 students, 6 mechanics, 2 insurance agents, a dean of a college of law, a physician, an attorney, a nurse, druggist, veterinarian, merchant, bookbinder, buttermaker, a worker in an ice-cream plant, a fisherman and an imbecile. There were 63 males and 20 females. Two cases only were under 13 years of age—a boy of 7 and a girl of 8. The oldest patient was 73 years of age. The infrequence of the disease in the young and the concentration of cases in the age group 20-49 is most striking. In those cases having no contact with stock the absence of such a grouping is apparent. With three exceptions the infection was clearly acquired within the State. In only five cases had the patient taken any but local trips within one year, and in no case had they been traveling in Southern states or in foreign countries within recent years. A study of the diet of the patients was made as to the individual consumption of dairy products and meats. There were 52 cases in which the evidence indicated that the infection was acquired from cattle. In the study of the cattle suspected of being the source of these infections presumptive or suggestive histories of contagious abortion were given in 21 instances and confirmary serological evidence was obtained. In 2 instances not even a suggestive history was elicited, but sera gave strong agglutination reaction. Another case was in a veterinarian who used raw milk but who also was treating several herds of cattle for contagious abortion. In 8 addition cases it was clearly evident that the condition of contagious abortion was in the herds, but serological examinations were not made. In 18 cases the milk was regularly purchased from a public dairy supplying raw milk, while in 2 cases pasteurized milk was ordinarily used, although extra supplies of raw milk were purchased from local stores. Serological tests were not practicable where public dairies received milk from several sources. Histories of the herds, however, were procured, and in 15 instances the infection was known to be present in some of the herds. A second group included 11 cases in which the evidence indicated that the infections were acquired from hogs, 5 being packing-house workers and 6 farmers. In a third group of 4 cases there was a known possible source in both cattle and hogs. In one case only did the evidence strongly suggest that the infection was secondary to a previous human case, and this patient was one of the two fatalities that occurred. In 15 cases no clear evidence of the source of the infection could be obtained. The mode of transfer of the organism from the infected animal to man is a matter of great importance. In 25 cases the evidence suggested that the organism was transmitted through raw milk or cream. In the case of the packing-house workers, it may be accepted that the organism was acquired either from the infected meat or from excreta, and gained entrance through the injured or unbroken skin, or by way of the digestive tract. The same would hold good for the other cases in which the infection was acquired from hogs. In the remaining cases it was impossible to determine the precise mode of transfer, although there are two possibilities, either through dairy products used as food or by contamination with infectious excreta from livestock. It is evident that those working around stock are exposed more dangerously than those using the same dairy products but not working with stock. It seems evident that a goodly proportion of the infections were acquired from contamination by animal body discharges. The

possibility that the organism may gain entrance through the skin, either abraded or apparently normal, must be recognized. There was no evidence obtained from the Iowa cases that the infection was in any case acquired from goats, sheep or horses. The clinical symptoms of the Iowa cases showed a marked variation in symptomatology and physical findings, as is characteristic of this disease. The onset was usually insidious, but in a few instances was sudden. The first symptom usually is weakness, and this is the only constant one. The most striking feature of the disease is profuse night sweating, but this not always present. Sensations of chilliness were very common, and rigors occurred in the severe cases. General aching, headache, backache, and arthralgia accounted for most of the pain. Anorexia, succeeded by a good appetite, even in the presence of fever, was common. Constipation was the rule. Insomnia, irritability and apprehension was the usual nervous disturbances. Secondary bronchitis sometimes occurred. The patients often did not feel ill. In more than half of the cases no abnormal physical findings were detected, but a palpable spleen and epigastric tenderness were often noted. The temperature was irregular and intermittent, usually with morning remissions, often to normal. In less than one-third of the cases were there known undulations with periods of apyrexia. The total white count tended toward a slight leucopenia; the differential usually showed a decrease in polymorphonuclears with a corresponding increase in mononuclears. The course, which covered a period of three weeks to nine months, was marked by a progressive loss of weight and an anemia. Arthritis, orchitis, mastitis and cardiac disturbances were infrequent complications. The case varied in severity from an ambulatory to a malignant type; but the intermittent form with relatively mild persistent symptoms was common. No case was included in which an agglutination of *Br. melitensis* in a titer of at least 1:80 was not obtained. Of the 83 cases studied a higher titer than this was obtained in 78 (94 per cent). In 46 cases there was complete agglutination in a serum dilution of 1:1280 or higher; in 9 cases there was complete agglutination in the 1:5120 dilution. The agglutinins were repeatedly observed to increase during the course of the disease and slowly to decreased following convalescence. Bacteriological study could be made on only a few cases. In 9 patients *Br. melitensis* was, however, isolated from the blood; and from five of the seven cases studied in hospitals the cultures were positive. The grouping of the organisms isolated from the patients has yet to be done. The prevention of the disease cannot be brought about wholly by the pasteurization of milk. The disease is also an occupational one in packing-house workers and in those handling stock. In these the prevention of the disease will be dependent upon the control of the infection in animals and in precautions taken on the part of those handling stock. In the packing house cases the disease is clearly an occupational one; these patients have been unable to work for a period varying from 1-5 months. For compensation to be obtained by workmen acquiring this infection it must be recognized that undulant fever among packing-house workers is an occupational disease.

Reviews

Blood and Urine Chemistry. By B. H. GRADWOHL, M.D., Director of the Gradwohl Laboratories, St. Louis, Mo.; and IDA E. GRADWOHL, A.B., Instructor in the Gradwohl School of Laboratory Technic, St. Louis, Mo. 542 pages, 117 illustrations and 4 color plates. The C. V. Mosby Company, St. Louis, Missouri, 1928. Price in cloth, $10.00.

This volume is intended to be a textbook for laboratory workers and practitioners of medicine. The methods are set forth as clearly as possible, following the plan used by the authors in the instruction of laboratory technicians, and are standard and up to date. They are explained in detail so that the book may be a useful working manual in the laboratory; these explanations are given in simple style, the calculations in the proper form, and there is a full explanation of the apparatus required in the performance of these various tests. The book is divided into four parts: Part I, Technic of Blood Chemistry; Part II, Chemistry of Urine; Part III, The Interpretation of Blood Chemical Findings; and Part IV, Basal Metabolism. The methods given under these different sections are very complete and up-to-date. The authors emphasize the practical importance of blood chemical methods in both surgical and medical practice. There is hardly a specialty in medicine in which these methods are not of importance in the summing up of the individual's disability, as they touch upon the integrity of liver and kidney function, upon internal glandular secretory activity, upon operative risk, and upon all that goes with metabolic function and dysfunction. In the estimation of operative risks blood chemical tests have shown their great importance. This volume offers a most convenient compilation of all the most important chemical tests, and should be of service to the laboratory worker. The book is well printed, is easily and conveniently read, and the illustrations, while adequate, are fair.

The Conquest of Disease. By THURMAN B. RICE, A.M., M.D., Assistant Professor of Sanitary Science, Indiana University School of Medicine. 363 pages, 62 charts and figures. The MacMillan Company, New York, 1927. Price in cloth, $2.50.

The author states his purpose in writing this book to be: To set forth the most recent scientific information concerning the transmissible diseases to the end that these diseases may be controlled or perhaps ultimately eradicated; To make the subject interesting, if possible, to the general reader, and to such persons and students as may need to study the subject. The complete conquest of the transmissible diseases waits as much upon the intelligent appreciation of the facts by the laity, as it does upon the advances in research made by the medical profession; to emphasize the great advances that have already been made through scientific methods by comparing the past with the present. Confidence in the methods and motives of science is a most important asset to the people of the modern world, and in no field is its value more dearly demonstrated than in the conquest of disease. The discussions presented are accurate, based upon fact, and presented in simple, non-technical language. The expert can find no fault with this presentation of the victories of modern medical science over disease. The style is interesting and devoid of the hot-air or sophomoric vulgarity which has characterized other popular books of this kind. There is no attempt to be sensational; its pages are pervaded with a quiet decent sense of humor which places the book far ahead of such smarty attempts as DeKruif's

"Microbe Hunters." The romance of the fight against disease is presented in this volume more accurately than in the book just named, and with decency of treatment, without yellow-journalism appeal. Therefore, it is a book that should be read by all intelligent persons to whom the facts presented in it should become common knowledge and practically applied in daily life.

The Principles of Ante-Natal and Post-Natal Child Hygiene. By W. M. FELDMAN, M.D., B.S., M.R.C.P. (Lond.), F.R.S. (Edin.). Senior Physician to St. Mary's Hospital for Women and Children. 743 pages, 161 illustrations and 14 plates, including over 100 portraits. John Bale, Sons and Danielson, Ltd., London, 1927. Price in cloth, $7.00.

This book is intended to be a companion volume to the author's book on "The Principles of Ante-Natal and Post-Natal Child Physiology," with which it is published uniform in size and manner of treatment. It is a fore-runner in this field of preventive paediatrics, comprehensive in its treatment, and should appeal to every educated and thoughtful person, lay or medical, who is more than superficially interested in the welfare of children during their various phases of ante-natal and post-natal life. The volume is also designed as a work of reference for paediatrists, medical child welfare workers, and students engaged in original investigations concerned with the hygiene of child life. The material of the book comprises three parts: Prolegomena, Ante-Natal and Post-Natal Hygiene. In Part I the historical survey of child hygiene contains much interesting subject matter drawn from many sources and all intelligent and educated readers will find this profitable reading. Its 63 pages constitute a very valuable monograph on this subject. It is illustrated with the portraits of those workers who have made some valuable contribution to the development of child-hygiene, including not only medical men and research workers, but social workers as well. For all of these this volume is of great value as a reference book and a useful guide, as it summarizes critically and in considerable detail practically everything that has been accomplished in the various branches of Child Hygiene up to the time of publication. The biometrics of child hygiene, ante-natal and intra-natal mortality, child mortality and maternal mortality are fully discussed in Part I. In Part II, Heredity and Environment in their relation to child hygiene, the physiology of the fetus and the care of the expectant mother are given full attention. In Part III the physiology of early post-natal life, neo-natal hygiene, general nursery hygiene, the nutrition of the infant and the child, breast feeding, wet nursing, artificial feeding of infants and feeding of older children, clothing, muscular exercise, rôle of sunlight and its artificial substitutes, physiology and hygiene of the premature and congenitally debilitated infant, hygiene of the teeth and the sense organs, the prevention of infectious diseases, the physical and mental growth of the child, the mental hygiene of early life and adolescence of puberty form the chapter headings, and each of these subjects receives adequate treatment as far as our knowledge go. The most important facts of modern research are given clearly and concisively, with full reference to the original papers. There are numerous valuable charts and figures. The material brought together in this book is of the utmost importance, and should be known to every intelligent parent. It can be easily understood by any educated layman, and is recommended to such. The book is well printed, and the illustrations adequate.

A Textbook of Pharmacology and Therapeutics or The Action of Drugs in Health and Disease. By ARTHUR R. CUSHNY, M.A., M.D., LL.D., F.R.S., Late Professor of Materia Medica and Pharmacology in the University of Edinburgh. Ninth Edition, Thoroughly Revised, by C. W. EDMUNDS, A.B., M.D., Professor of Materia Medica and Therapeutics in the University of Michigan, Ann Arbor; and J. A. GUNN, M.A., M.D., D.Sc., Professor of Pharmacology in the University of Oxford, Oxford, England. 743 pages, 73 illustration. Lea

and Febiger, Philadelphia, 1928. Price in cloth, $6.00.

This classic work on the action of drugs and their applications in therapeutics had been constantly revised by Professor Cushny through eight editions. The rapid progress in experimental investigation and practical application in the field of therapeutics is strikingly shown in comparing these eight editions during the twenty-five years in which they appeared. In the eighth changes were made by Cushny in the chapters on digitalis and the cinchona bases, and on ergot. He also added new chapters on histamine action and the related symptoms of anaphylaxis and shock, and on the insulin treatment of diabetes, and on the vitamins. Changes were also made in the sections on cocaine, quinine, thyroid, strychnine and pituitary. These additions were compensated by the rearrangement and simplification of the chapters, and by the curtailment of the space given to obsolescent drugs. The test was also embellished with various references to drugs found in general literature. The immediate object of the present edition is to bring it intoline with the tenth edition of the United States Pharmacopoeia, and the opportunity has been utilized to bring the subject matter also up to date. The present revision has endeavored to maintain the critical spirit which was such a valuable feature of the book, and, wherever possible, the original text has also been preserved. The work of the revising editors has been most successfully accomplished. They have succeeded in prolonging the active life of Cushny's most valuable book—it remains still the leading textbook in pharmacology and therapeutics, and it will continue to fulfill the important rôle played by the preceding eight editions in its critical sifting and promulgation of the advance of knowledge in this field. In accomplishing this successful revision the editors have paid an adequate tribute to the memory of the author, and have extended the great influence which he had in the field of experimental and didactic pharmacology.

Bacteriology, General, Pathological and Intestinal. By ARTHUR ISAAC KENDALL, B.S., Ph.D., Dr. P.H. Professor of Research Bacteriology in the Northwestern University Medical School, Chicago, Illinois, Third Edition, Thoroughly Revised. 733 pages, 103 engraving and 8 plates. Lea and Febiger, Philadelphia, 1928. Price in cloth, $7.00.

Many notable and significant contributions to bacteriology and related subjects have been made since the last edition of this book. Therefore, thorough revision, much rewriting and the introduction of much new material has been necessary. The present moment is a transitional one in bacteriology, it is becoming a new science in many ways, and it is not possible at the present time to make safe predictions as to the future. This book seems to have lagged behind somewhat in the new developments in the field of bacteriology. There is very little about bacterial dissociation in this work—in fact this term is not even in the index. It is rather an old-fashioned type of bacteriology that is presented here—the cataloguing of various species and forms, as to morphology, cultural characteristics and pathogenic qualities; but there is very little of the modern knowledge of bacterial metabolism, cycles, transmutation, and involution, etc. The Kahn test, Dick test, scarlet fever antitoxin, filterable viruses, bacteriophage, filtration, etc., have been considered in this edition; but of the newer work and problems of bacteriology there is very little mention. Mellon's important work is not even mentioned. The author seems to have turned a blind eye or a deaf ear to the modern problems of bacterial biology that in recent years have received so much attention and discussion. The book is well printed, in convenient reading form and legible type, and the illustrations are adequate. The book is really more adapted to laboratory work than as a textbook covering the teaching field of bacteriology. Practical diagnostic application is emphasized rather than critical scientific discussions of the many perplexing phenomena that have been observed in the field of bacteriological investigation and which remain to be correlated before the natural history of bacterial life becomes intelligible.

College News Notes

THIRTEENTH ANNUAL CLINICAL SESSION, APRIL 8-12, 1929

Dr. Frank Bell Steele (Fellow), formerly of Salt Lake City, is now Medical Officer at the U. S. Veterans Hospital at Maywood, Illinois.

Dr. Stewart R. Roberts (Fellow), Atlanta, Ga., has been made Chairman of a Committee to write the History of Medical Education in Georgia.

Dr. Ralph Kinsella (Fellow), has recently received the appointment as Professor of Internal Medicine of the St. Louis University Medical School.

Dr. L. R. DeBuys (Fellow), New Orleans, La., has been elected President of the Louisiana State Pediatric Society for the present year.

Dr. I. I. Lemann (Fellow), New Orleans, La., is author of an article entitled "Nephritis in Children and Young Adults with Especial Reference to Focal Glomerulo-Nephritis," appearing in the September issue of the Southern Medical Journal.

Dr. Orlando H. Petty (Fellow), Philadelphia, Pa., is author of a Handbook for the Patient, entitled "Diabetes, Its Treatment by Insulin and Diet," published by F. A. Davis Company. This is the fourth revised and enlarged edition and contains an introductory foreword by Dr. John B. Deaver.

Dr. Frank P. Norbury (Fellow), Jacksonville, Ill., addressed the Christian County Medical Society at Taylorville, July 19, on "Evolution in Diagnostic Methods."

At the Annual Meeting of the Eighth District Medical Association at Atlanta, Dr. Allen H. Bunce (Fellow) and Dr. Stewart R. Roberts (Fellow) were among the principal speakers.

Dr. David J. Davis (Fellow), Dean of Illinois School of Medicine, and Dr. Julius H. Hess (Fellow), Professor of Pediatrics at the same institution, are members of a Committee to "consider the present status of work on vaccination against tuberculosis with the Bacillus Calmette-Guérin, and especially the application of the method of vaccination to the general public by the Chicago Municipal Tuberculosis Sanitarium, where this organism has been studied by animal experimentation for about one year," according to the Journal of the American Medical Association.

Dr. Edwin C. Ernst (Fellow), St. Louis, Mo., represented The Radiological Society of North America at the International Congress on Radiology at Stockholm, Sweden, during last July.

Dr. Albert Soiland (Fellow), Los Angeles, Calif., attended the International Congress on Radiology at Stockholm, Sweden, as a delegate from The American Radium Society.

Dr. B. H. Orndoff (Fellow), Chicago, Illinois, organized a party of sixty-seven American Radiologists, mostly from The Radiological Society of North America, to attend the International Congress on Radiology held at Stockholm, Sweden. Dr. Orndoff attended the Congress as a delegate from The American College of Radiology.

Dr. I. S. Trostler (Fellow), Chicago, Ill., addressed the Oneida-Forest-Vilas

County Medical Society at Rhinelander, Wisconsin, on August 3, on "Some of the Less Known Uses of Roentgenotherapy."

Dr. Maximilian J. Hubeny (Fellow), Chicago, Ill., presented "The Rôle of Roentgenology in Psychiatry" at the recent meeting of The American Roentgen Ray Society at Kansas City, Missouri.

Dr. John L. Chester (Fellow), Detroit, Mich., who is chief of the visiting staff at Eloise Hospital, Eloise, Mich., was recently appointed an attendant on medical service at Providence Hospital, Detroit. Dr. Chester spoke before Michigan State Medical Society at Detroit on September 28th on "Electrocardiograms and Their Clinical Significance," having previously addressed Tri-County Medical Society at St. Louis, Mich., September 6th, on the subject of "Rheumatic Heart Disease."

Dr. George M. Kober (Fellow), Washington, D. C., retired as Dean of the Georgetown University School of Medicine, Washington, on September 18, after twenty-seven years' service. Dr. Kober has been placed on the Board of Regents of the University and made Dean Emeritus of the Medical School. He is one of the founders of Georgetown Hospital, and was formerly President of the Association of American Medical Colleges and also of the Medical Association of the District of Columbia.

The Graduate Department of the University of Michigan and the Michigan State Medical Society conducted postgraduate clinics at Grand Rapids, Flint and Jackson, Michigan, during October. Dr. Martin A. Mortensen, Battle Creek, Dr. Frank Smithies, Chicago, Dr. James D. Bruce, Ann Arbor, and Dr. Walter C. Alvarez, Rochester, Minnesota, all Fellows of The College, were among the speakers at these postgraduate clinics.

Dr. James H. Means (Fellow), Boston, and Dr. Warfield T. Longcope (Fellow), Baltimore, were among the speakers at a series of afternoon lectures sponsored by the Medical School of Harvard University at Boston, during October.

Dr. J. Gurney Taylor (Fellow), Milwaukee, was elected a delegate to the American Medical Association at the recent annual meeting of the State Medical Society of Wisconsin in Milwaukee.

Dr. George W. F. Rembert (Fellow), Jackson, addressed the Issaquena-Sharkey-Warren Counties Medical Society at Vicksburg, Miss., on the subject "Vincent's Infection of the Gums," on September 11.

Dr. Henry Boswell (Fellow), Sanatorium, Miss., Dr. Felix J. Underwood (Fellow), Jackson, Miss., and Dr. L. J. Moorman (Fellow), Oklahoma City, Okla., addressed the Southern Tuberculosis Conference and Southern Sanatorium Association at Biloxi, Miss., September 12-15.

Dr. Solomon L. Cherry (Fellow), Clarksburg, W. Va., addressed the Central West Virginia Medical Society, September 19, on "Medical and Dental Coöperation."

Dr. Charles A. Ray (Fellow), Charleston, W. Va., past President of the State Medical Association of West Virginia, arranged the scientific program for the meeting of the Fayette County Medical Society at Charleston on August 14. Dr. Arthur A. Shawkey (Associate) spoke before the meeting on "Colic in Infants."

Dr. Rock Sleyster (Fellow), Milwaukee, a member of the Board of Governors of The American College of Physicians and a member of the Board of Trustees of the American Medical Association, addressed the Eleventh Councilor District Society at Ashland, August 9, on "Psychiatry and the General Practitioner."

Dr. Arthur R. Elliott (Fellow), Chicago, was one of the speakers at the Third District Medical Society Meeting at Madison, Wisconsin, on October 12.

Dr. George Piness (Associate), Los Angeles, was made President-Elect of the

American Association for the Study of Allergy at Oakland, Calif. Dr. Ray M. Balyeat (Fellow), Oklahoma City, was elected Vice-President of the same Association.

At the Clinical Congress of The American College of Surgeons held in Boston, October 8-12, the following members of The American College of Physicians appeared on the program:

Dr. J. H. Means (Fellow) et al,—Dry Clinic on "Demonstration of Methods of Treatment of Fractures, and Demonstration of Cases."

Dr. Henry A. Christian (Fellow),—"Missed Pedagogic Opportunities Incident to the Usual Organization of the Resident Medical Staff of the Hospital" and Dry Clinic on "Medical Diagnostic and Therapeutic Clinic."

Dr. Joseph C. Doane (Fellow), Philadelphia,—"Measuring the Professional Efficiency of the Hospital."

Dr. Josiah J. Moore (Fellow), Chicago,—"Relation of the Clinical Pathologist to the Medical Staff and the Scientific Work of the Hospital."

Dr. Franklin W. White (Fellow),—Dry Clinic on "Intussusception of the Bowel occurring within the Stomach following Gastro-enterostomy."

Dr. Myrtelle Canavan (Fellow), Curator of the Warren Museum, Harvard Medical School—Demonstrations.

Dr. Elliot P. Joslin (Fellow) et al,—Dry Clinic on "The Treatment of Diabetic Feet."

Dr. Joseph H. Pratt (Fellow),—"Chronic Appendicitis, Differential Diagnosis."

Dr. Christopher G. Parnall (Fellow), Medical Director, Rochester General Hospital, Rochester, New York, was elected President-elect of the American Hospital Association at the annual meeting held in San Francisco August 6-10, 1928. Dr. Parnall was recently appointed consultant to the Sealy and Smith Foundation of Galveston, Texas, and also consultant to the Board of Health of the City of Indianapolis on the building program for several new units of the Indianapolis City Hospital.

The following are a few of the new publications for 1928 by Fellows of The American College of Physicians:

Laennec, A Memoir. By GERALD B. WEBB, M.D., President, Colorado School of Tuberculosis, Colorado Springs; U. S. Government Delegate to the Laennec Centenary, Paris, December, 1926. 146 pages, with 13 full page plates. New York: Paul B. Hoeber, Inc.

Recent Advances in Chemistry in Relation to Medical Practice. By W. MCKIM MARRIOTT, B.S., M.D., Dean and Professor of Pediatrics, Washington University School of Medicine. 141 pages, illustrated. St. Louis: C. V. Mosby Company.

General Therapeutics. By BERNARD FANTUS, M.S., M.D., Associate Clinical Professor of Medicine, Rush College of the University of Chicago; Member, Revision Committee United States Pharmacopoeia and of National Formulary Revision Committee. Chicago: The Year Book Publishers.

Rules for Recovery from Pulmonary Tuberculosis. By LAWRASON BROWN, M.D. Fifth Edition. Thoroughly Revised; 244 pages. Philadelphia and New York: Lea & Febiger.

Diabetic Manual for Patients. By HENRY J. JOHN, M.A., M.D., Major, M.R.C., Director of the Diabetic Department and Laboratories of the Cleveland Clinic. 202 pages, illustrated. St. Louis: C. V. Mosby Company.

The Treatment of Diabetes Mellitus. By ELLIOTT P. JOSLIN, M.D. (Harvard), M.A. (Yale), Clinical Professor of Medicine, Harvard Medical School. Fourth Edition. Enlarged, revised and rewritten. 998 pages, illustrated. Philadelphia and New York: Lea & Febiger.

Dr. Allen H. Bunce (Fellow), as Secretary of the Medical Association of Georgia, is managing a package library service at the A. W. Calhoun Medical Library, Emory University, Atlanta, whereby members of the Association may obtain material on various subjects.

Dr. Hugh S. Cumming (Fellow), Surgeon-General of the U. S. Public Health Service, has been elected a corresponding member of the Royal Society of Medicine of Great Britain.

Dr. George Harlan Wells (Fellow), Philadelphia, presented a paper on "Drugs as Antigens" before a symposium on chemotherapy at the Philadelphia County Medical Society on September 26. Dr. Solomon Solis-Cohen (Fellow), Philadelphia, appeared on the program as a discusser, "From the Viewpoint of the Internist."

At the annual meeting of the Gibson County (Tennessee) Medical Society at Trenton, Tenn., August 21, Dr. W. Calvert Chaney (Fellow), Memphis, read a paper on "Diagnosis of Diseases of the Thyroid," illustrated with slides; and Dr. Henry Rudner (Fellow), also of Memphis, discussed "Vincent's Disease."

Under the presidency of Dr. George D. Porter (Fellow), Toronto, the Canadian Public Health Association held its annual session in Winnipeg, October 11-13.

Dr. Joseph C. Doane (Fellow), Philadelphia, after fourteen years in various capacities with the Philadelphia General Hospital, severed his connection as Superintendent of that institution on October 1 to become Medical Director and Visiting Physician on the medical service of the Jewish Hospital.

During Dr. Doane's administration, many interesting and epochal changes have been brought about at the Philadelphia General Hospital. Only last December were the new buildings dedicated. These six new units, erected at a cost of about five million dollars, added twelve hundred and fifty beds to the hospital plant. There are total accommodations in all buildings for twenty-six hundred patients, the largest city institution in America.

Dr. Doane, as the new Medical Director of the Jewish Hospital, has been making plans for the introduction of graduate teaching in this institution for the first time in its existence. He has expressed the hope of receiving graduate classes from the University of Pennsylvania into the wards of the Jewish Hospital for teaching purposes.

The Carpenter Lecture of the New York Academy of Medicine for 1928 was delivered by Dr. Aldred Scott Warthin, at the Academy on October 1, on "The Pathology of the Aging Process."

Dr. Harlow Brooks spoke on "Angina Pectoris" before the Graduate Fortnight meeting at the New York Academy of Medicine October 11, 1928.

OBITUARIES

Dr. Ralph Campbell (Fellow, February 14, 1920) died in Los Angeles, August 18, 1928, aged 61. He was a graduate of the Jefferson Medical College of Philadelphia, 1890, and did post-graduate study in Germany. Dr. Campbell was, at one time, professor of Dermatology at the College of Medical Evangelists, Los Angeles, and was formerly Secretary and Chairman of the Section of Dermatology of the American Medical Association. From 1908 to 1909, he was a member of the House of Delegates of the same Association. During a residence in Chicago he had staff connections with Cook County, Henrotin and Polyclinic Hospitals. In Los Angeles he had been on the staff of the Los Angeles General and the White Memorial Hospitals. Besides being a Fellow of the American College of Physicians, he was a member of his county and state medical associations, a Fellow of the American Medical Association, and a member of the American Dermatological Association. Dr. Campbell's pleasing personality had made him a host of friends who, with the members of his profession, mourn his passing.

Dr. Samuel W. Welch (Fellow), Talladega, Alabama; died August 20, 1928, of cardio-vascular disease.

In the death of Dr. Samuel W. Welch, State Health Officer of Alabama, the American College of Physicians loses one of its most distinguished Fellows. Dr. Welch was born February 14, 1861, and received his collegiate education at Howard College, with the degree of B.S. in 1881. He graduated in medicine at the College of Physicians and Surgeons of Baltimore in 1893; and later did post-graduate work at Johns Hopkins and Columbia Universities. He was in general practice at Talladega, Alabama, for a number of years, but throughout his career was interested in public health, having been a member of the Alabama State Board of Health since 1903. He was elected State Health Officer of Alabama in 1917 and made a very remarkable record in the upbuilding of a most efficient state health department, so that Alabama's public health system is regarded as the best in the United States. As a result of appropriations secured by Dr. Welch from the State Legislature, Alabama has the largest number of full county health units of any state in the Union, and within the next year each of the sixty-seven counties of Alabama will have a full-time health officer with a complete health unit.

Dr. Welch received many honors at the hands of his professional confreres, having been President of the State Medical Association in Alabama, President of the Association of Health Authorities of North America, and had he lived, would probably have been elected President of the American Medical Association at its next meeting. He was also a member of the American Public Health Association and the Southern

Medical Association. He was elected a Fellow of The American College of Physicians on March 10, 1925, and has been an enthusiastic and helpful member since that time. Dr. Welch was the author of a large number of articles dealing with all phases of public health administration.

Dr. Welch served as State Chairman of the Committee on National Defense, Medical Section, during the World War, and was also Chairman of the National Malaria Commission. His death took place at Montgomery, Alabama, on September 20, 1928, following a brief illness, though for some months he had been known to have cardio-vascular disease.

(Furnished by Dr. Seale Harris, Governor for Alabama)

"Dr. George Palmer McNaughton (Fellow, February 22, 1921), Chief of the Medical Department of the Jefferson Clinic and Diagnostic Hospital of Detroit, Michigan, died of heart disease on August 21, 1928, while on a vacation near Gladwin, Michigan.

Dr. McNaughton was born in Ottawa, Ontario, in 1878, and received his early education in Milwaukee. He graduated from Rush Medical School in 1900 and served for two years as Resident Physician in Cook County Hospital. Dr. McNaughton became Chief of Internal Medicine at the Jefferson Clinic in 1919 and has participated actively in the development of that institution. Previously he enjoyed large practices in Sault Ste. Marie and later at Standish, Michigan. He served for five years at Attending Physician to St. Mary's Hospital, was Associate Professor of Medicine in the Detroit College of Medicine and Surgery, and Consultant in Internal Medicine and Chairman of the Executive Committee of the staff of Receiving Hospital. He was elected a Fellow of The American College of Physicians in 1921.

Aside from his ability as a clinician, he had a charming personality. His imposing physique, his joy of living, his cheery manner, his great heartedness made him friends everywhere and in every company. Genial and dignified, he was the embodiment of courtesy, and his widespread interests made him a delightful companion. A generous kindness characterized everything he did. There are few men who have as many friends. His death will make his colleagues, and the profession, the poorer by the loss of a personality always enthusiastic, considerate and kind."

LIFE MEMBERS

The Constitution and By-Laws provide: "In lieu of annual dues a Master or Fellow may become a Life Member of The College upon the payment of $500 in cash, or $100 each year until $500 has been paid. In case a member desires to pay for life membership by paying $100 yearly for five years, his annual dues shall cease when he has made three annual payments of $100 each."

Life membership, of course, includes waiver of all subsequent fees, full membership privileges for life, benefits of the Clinical Session and the receipt of all official publications of The College, including ANNALS OF INTERNAL MEDICINE. A wise provision of the By-Laws is that all moneys received for life membership in The College shall be added to the permanent endowment fund, the principal of which shall be held intact and invested in securities approved by the Board of Regents, while the income only shall be available for meeting current expenses of the organization.

The life membership movement deserves the highest commendation and offers a source for a permanent endowment for the perpetuation of the work of The College. More Fellows should be interested in seeking life membership. The present life members are:

Lewellys F. Barker.....Baltimore, Md.
Oscar Berghausen.....Cincinnati, Ohio
Carl R. Comstock..Saratoga Springs, N. Y.
Charles F. Martin..Montreal, Que., Canada
Nels C. Meling.....Evanston, Ill.
John Phillips.....Cleveland, Ohio
Adolph Sachs.....Omaha, Nebr.
Frank Smithies.....Chicago, Ill.
Alfred Stengel.....Philadelphia, Pa.
Noxon Toomey.....St. Louis, Mo.
M. L. Turner.....Berwyn, Md.
Alonzo H. Waterman.....Chicago, Ill.
Bernard L. Wyatt.....Tucson, Ariz.

THE COLLEGE LIBRARY

Through the gifts of a considerable number of the members of The College, more than one hundred volumes have been added to The College Library in the Executive Offices.

All members of The College who are authors or co-authors of books are requested to present a copy to The College, in order that a complete collection of all the books our members have produced or to which they have contributed may be made.

Books sent to the Executive Offices of The College are immediately indexed with the names of the donor and the date of the gift.

1928 SUPPLEMENT TO YEAR BOOK

During the summer months, Mr. Loveland, the Executive Secretary, and his staff prepared the Supplement to the 1927-28 YEAR BOOK, and distributed same to all members of The College in good standing.

The Board of Regents of The College has determined the policy of issuing a complete Year Book every two years. Inasmuch as the regular edition for 1927-28 was printed during the summer of 1927, this Supplement was issued only to include new members elected since the publication of the last Year Book. It is necessary, therefore, to use the Supplement along with the Year Book proper to have a complete directory of all members of The College. During 1929, it is anticipated a new complete edition of the Year Book will be issued.

The Executive Offices still have in stock available copies of both the Year Book and the Supplement for distribution to those who wish to place orders. Supplement $.50, postpaid; Year Book $1.00, postpaid.

THIRTEENTH ANNUAL CLINICAL SESSION of THE COLLEGE

Boston, Mass., April 8-12, 1929

Dr. James H. Means, General Chairman of Arrangements for the next Annual Clinical Session of The College at Boston, reports the following:

"The headquarters for the Boston meeting will be the Hotel Statler. The scientific sessions will be held in its ballroom in the afternoons and evenings. The pro-

gram for the scientific session is well in hand and there are already promises from a very representative group of distinguished Internists from all over the United States and Canada, some Fellows of The College, others guests. One of the items that bids fair to be of especial interest is a symposium on deficiencies—deficiencies of all sorts to be considered as a class of agencies productive of acute and chronic disease on a par, for example, with infections. This will be opened by Dr. George R. Minot who will speak on some of the fundamental aspects of deficiencies. Dr. Minot will be followed by Dr. S. Burt Wolbach who will speak on the pathology of deficiencies, by Dr. Joseph Goldberger on pellagra, Dr. Randolph West on pernicious anemia, and Dr. Edward J. Wood on sprue.

"Dr. Benjamin White of the Massachusettes Department of Health will give an hour's lecture one of the evenings upon a critical review of sera and vaccines in the prophylaxis and treatment of disease, the idea being to give the Internist the last word on just where we stand on specific immunologic procedures.

"Dr. Homer Swift has promised to speak briefly on rheumatic fever and Dr. James B. Murphy on cancer. We also find on the program many speakers bound to be very welcome to The College, such as Dr. Lawrason Brown, Dr. David Riesman, Dr. J. C. Meakins, Dr. L. F. Barker, Dr. J. B. Herrick, and many others."